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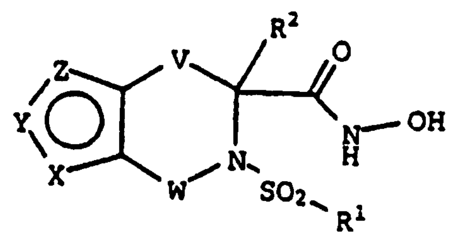
(54) Title: HYDROXAMIC ACID SUBSTITUTED FUSED HETEROCYCLIC METALLOPROTEINASE INHIBITORS

(57) Abstract

Selected novel hydroxamic acid substituted fused heterocyclic compounds of formula (I) are effective for prophylaxis and treatment of inflammation, tissue degradation and related diseases. The invention encompasses novel compounds, analogs, prodrugs and pharmaceutically acceptable salts thereof, pharmaceutical compositions and methods for prophylaxis and treatment of inflammation, tissue degradation and related diseases. The subject invention also relates to processes for making such compounds as well as to intermediates useful in such processes (I).



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HYDROXAMIC ACID SUBSTITUTED FUSED HETEROCYCLIC METALLOPROTEINASE INHIBITORS

BACKGROUND OF THE INVENTION

This application claims the benefit of U.S. Provisional Application No. 60/054,753 filed August 4, 1997, which is hereby incorporated by reference. The present invention relates to metalloproteinase inhibitors and more particularly, relates to novel compounds, composition and method for prophylaxis and treatment of inflammation, tissue degradation and the like. This invention, in particular, relates to novel hydroxamic acid substituted fused heterocyclic compounds, compositions containing such compounds and methods of use of such compounds. The subject invention also relates to processes for making such compounds as well as to intermediates useful in such processes.

Metalloproteinase enzymes, such as collagenases (e.g., MMP-1, MMP-8 and MMP-13), stromelysins (e.g., MMP-3, MMP-10, MMp-11 and MMP-7), gelatinases (e.g., MMP-2 and MMP-9) and TNF convertase, may contribute to the onset, etiology, or exacerbate disease states which are related to connective tissue degradation, secretion of proinflammatory cytokines and the like. For example, matrix metalloproteinases, such as collagenases, stromelysins and gelatinases, are thought to be involved in the tissue breakdown observed in rheumatoid arthritis; osteoarthritis; osteopenias (e.g., osteoporosis); periodontitis; gingivitis; corneal, epidermal and gastric ulceration; and tumour metastasis, invasion and growth; in neuroinflammatory disorders, such as myelin degradation (e.g., multiple sclerosis); and in angiogenesis dependent diseases, such as arthritic conditions; solid tumor growth; psoriasis;

proliferative retinopathies; neovascular glaucoma; ocular tumours; angiofibromas; and hemangiomas.

Tumor Necrosis Factor alpha (TNF-α) is a proinflammatory cytokine secreted by a variety of cells including monocytes and macrophages in response to many inflammatory stimuli (e.g. lipopolysaccharide - LPS) or external cellular stress (e.g. osmotic shock, peroxide). Elevated levels of TNF play a major role in mediating many inflammatory disease states. Elevated levels of TNF-α may contribute to the onset, etiology, or exacerbate the following disease states: rheumatoid arthritis; osteoarthritis; rheumatoid spondylitis; gouty arthritis; inflammatory bowel disease; adult respiratory distress syndrome (ARDS); psoriasis; Crohn's disease; allergic rhinitis; ulcerative colitis; anaphylaxis; contact dermatitis; asthma; antiviral therapy including those viruses sensitive to TNF-α inhibition - HIV-1, HIV-2, HIV-3, cytomegalovirus (CMV), influenza, adenovirus, and the herpes viruses including HSV-1, HSV-2, and herpes zoster; muscle degeneration; cachexia; Reiter's syndrome; type II diabetes; bone resorption diseases; graft vs. host reaction; ischemia reperfusion injury; atherosclerosis; brain trauma; Alzheimer's disease; multiple sclerosis; cerebral malaria; sepsis; septic shock; toxic shock syndrome; fever and mylagias due to infection.

Several approaches have been taken to block the effects of TNF-α. One approach involves utilizing soluble receptors for TNF-α (e.g., TNFR-55 or TNFR-75) which have demonstrated efficacy in animal models of TNF-α mediated disease states. A second approach to neutralizing TNF-α utilizing a monoclonal antibody specific to TNF-α, cA2, has demonstrated improvement in swollen joint count in a Phase II human trial of rheumatoid arthritis (Feldmann et al Immunological Reviews p.195-223 (1995)).

The above approaches block the effects of TNF-α by either protein sequesterazation or receptor antagonism, but an additional approach to blockade is to intervene in the cellular secretion of TNF. TNF convertase is thought to be a metalloproteinase enzyme involved in the cellular secretion of TNF-α (Mohler et al., Nature 370:218-220, 1994; Gearing et al., Nature 370:555-557, 1994; McGeehan et al., Nature 370:558-561, 1994). Inhibition of TNF convertase is thought to be an additional approach to intervene in the cellular secretion of TNF-α. For example, a metalloproteinase inhibitor was shown to inhibit cellular secretion of TNF-α, in vitro and in vivo, which was thought to be due to inhibition of TNF convertase (McGeehan et al., Nature 370:558-561, 1994). WO 92/02822, WO 94/00555, WO 95/24501, WO 96/41624, WO 98/02557 and US Pat. 5,594,106 (each of which is incorporated herein by reference in its entirety) describe a TNF-α convertase and methods of identifying inhibitors thereof. While evidence as to the nature of intervention by metalloproteinase inhibitors in the cellular secretion of TNF-α exists, additional or alternative mechanisms of action by which such compounds inhibit TNF secretion may be involved, such as by intervening at a point on the pathway between extracellular stimulus and secretion of protein.

Since TNF-α is upstream in the cytokine cascade of inflammation wherein elevated levels of TNF-α lead to elevated levels of other cytokines including IL-1, IL-6 and IL-8, inhibiting the secretion of TNF-α may also reduce levels of other cytokines including but not limited to IL-1, IL-6 or IL-8.

Further, TNF-α is thought to play a role in head trauma, stroke, and ischemia. For instance, in animal models of head trauma (rat), TNF-α levels increased in the contused hemisphere (Shohami et al J. Cereb. Blood

Flow Metab. 14:615-619 (1994)). In an model of ischemia wherein the middle cerebral artery was occluded in rats, the levels of mRNA of TNF-α increased (Feurstein et al Neurosci. Lett. 164:125-128 (1993)). Administration of TNF-α into the rat cortex resulted in significant PMN accumulation in capillaries and adherance in small blood vessels. TNF-α promotes the infiltration of other cytokines (IL-1b, IL-6), and also chemokines, which promote neutrophil infiltration into the infarct area (Feurstein Stroke 25:1481-1488 (1994)).

TNF-α may also play a role in promoting certain viral life cycles and disease states associated with them. For instance, TNF-α secreted by monocytes induced elevated levels of HIV expression in a chronically infected T cell clone (Clouse et al, J. Immunol. 142:431 (1989)). The role of TNF-α in the HIV associated states of cachexia and muscle degradation has been discussed (Lahdevirta et al The American J. Med. 85:289 (1988)).

WO 97/18194 generically discloses N-(substituted-sulfonyl) thienyl-fused 5-7 membered ring nitrogen containing heterocycle hydroxamic acid compounds for use as inhibitors of matrix metalloproteinases and TNF production.

DE 3529960 and DE 3705220 disclose heterocyclic-fused-tetrahydropyridinyl-2-carboxylic acid derivatives, such as thieno-fused-tetrahydropyridinyl-2-carboxylic acid compounds, preparation and use as angiotensin I converting enzyme inhibitors.

DE 2800596 discloses the preparation and use for inhibition of agglutination of blood platelets, erythrocyte adhesion and thrombosis of thieno-fused-tetrahydropyridinyl-2-carboxylic acid derivatives.

DE 2812950 disclose the preparation and use for inhibition of agglutination of blood platelets, erythrocyte adhesion, thrombosis, pain and inflammation of thieno-fused-dihydropyridinone derivatives.

DE 2949399 discloses the use of thieno-fused-tetrahydropyridine derivatives as intermediates in the preparation of (thieno-fused-tetrahydropyridyl)-fused-tetrahydrothiazole compounds for use as antiviral, analgesic, antipyretic and anti-inflammatory agents.

FR 2457869 discloses the use of thieno-fused-tetrahydropyridinyl-2-carboxylic acid derivatives as intermediates in the preparation of (thieno-fused-tetrahydropyridyl)-fused-pyrazine compounds for use as sedatives.

WO 96/33172 discloses N-arylsulfonyl and N-heteroarylsulfonyl substituted 6 membered ring heterocycle hydroxamic acid derivatives, such as N-arylsulfonyl- and N-heteroarylsulfonyl-piperidinyl-2-hydroxamic acid compounds, preparation and use as inhibitors of matrix metalloproteinases and TNF production.

EP 606046 discloses N-arylsulfonyl and N-heteroarylsulfonyl substituted 5-6 membered ring heterocycle hydroxamic acid derivatives, such as N-arylsulfonyl- and N-heteroarylsulfonyl-piperidinyl-2-hydroxamic acid compounds and N-arylsulfonyl- and N-heteroarylsulfonyl-1,2,3,4-tetrahydroisoquinolinyl-2-hydroxamic acid compounds, preparation and use as inhibitors of matrix metalloproteinases.

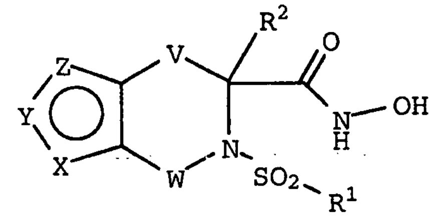
BRIEF DESCRIPTION OF THE INVENTION

The present invention relates to selected metalloproteinase inhibitory compounds, analogs and pharmaceutically acceptable salts and prodrugs thereof. The subject compounds are characterized as hydroxamic acid substituted fused heterocyclic compounds. The invention compounds useful in the prophylaxis and treatment of inflammation, tissue degradation and related diseases. Therefore, this invention also encompasses pharmaceutical compositions and methods for

prophylaxis and treatment of inflammation, tissue degradation and related diseases. The subject invention also relates to processes for making such compounds as well as to intermediates useful in such processes.

DETAILED DESCRIPTION OF THE INVENTION

In accordance with the present invention, there is provided a compound of the Formula:



(I)

or a pharmacutically acceptable salt thereof, wherein

R^1 is (1) an alkyl, alkenyl, alkynyl, cycloalkyl or heterocyclyl radical optionally substituted by 1-3 radicals of -OH, $-OR^3$, $-SR^3$, $-S(O)R^3$, $-S(O)_2R^3$, $-C(O)R^3$ or $-NR^3R^4$, aryl, heteroaryl, cycloalkyl or heterocyclyl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl, cycloalkyl and heterocyclyl radicals are optionally substituted by 1-3 radicals of hydroxy, $-OR^3$, $-SR^3$, $-S(O)R^3$, $-S(O)_2R^3$, $-C(O)R^3$, $-NR^3R^4$, amino, alkanoylamino, alkylsulfonylamino, alkoxycarbonylamino, alkoxycarbonyl, cyano, halo, azido, alkyl or haloalkyl;

preferably, R^1 is (1) an C_1-C_{12} alkyl, C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, cycloalkyl or heterocyclyl radical optionally substituted by 1-3 radicals of -OH, $-OR^3$, $-SR^3$, $-S(O)R^3$, $-S(O)_2R^3$, $-C(O)R^3$, $-NR^3R^4$, aryl, heteroaryl, cycloalkyl or heterocyclyl; or (2) aryl or

heteroaryl radicals; wherein the aryl, heteroaryl, cycloalkyl and heterocyclyl radicals are optionally substituted by 1-3 radicals of hydroxy, $-OR^3$, $-SR^3$, $-S(O)R^3$, $-S(O)_2R^3$, $-C(O)R^3$, $-NR^3R^4$, amino, C_1-C_8 alkanoylamino, C_1-C_8 alkylsulfonylamino, C_1-C_8 alkoxycarbonylamino, C_1-C_8 alkoxycarbonyl, cyano, halo, azido, C_1-C_8 alkyl or C_1-C_8 haloalkyl of 1-3 halo radicals;

more preferably, R^1 is (1) an C_1-C_{12} alkyl, C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, cycloalkyl or heterocyclyl radical optionally substituted by 1-3 radicals of -OH, $-OR^3$, $-SR^3$, $-S(O)R^3$, $-S(O)_2R^3$, $-C(O)R^3$, $-NR^3R^4$, aryl, heteroaryl, cycloalkyl or heterocyclyl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl, cycloalkyl and heterocyclyl radicals are optionally substituted by 1-3 radicals of hydroxy, $-OR^3$, $-SR^3$, $-S(O)R^3$, $-S(O)_2R^3$, $-C(O)R^3$, $-NR^3R^4$, amino, C_1-C_4 alkanoylamino, C_1-C_4 alkylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_6 alkyl or C_1-C_4 haloalkyl of 1-3 halo radicals;

more preferably, R^1 is (1) an C_1-C_{12} alkyl or cycloalkyl radical optionally substituted by 1-3 radicals of -OH, $-OR^3$, $-SR^3$, $-S(O)R^3$, $-S(O)_2R^3$, $-C(O)R^3$, $-NR^3R^4$, aryl, heteroaryl, cycloalkyl or heterocyclyl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl, cycloalkyl and heterocyclyl radicals are optionally substituted by 1-3 radicals of hydroxy, $-OR^3$, $-SR^3$, $-S(O)R^3$, $-S(O)_2R^3$, $-C(O)R^3$, $-NR^3R^4$, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4

alkoxycarbonyl, cyano, halo, C_1-C_6 alkyl or $-CF_3$ radicals;

more preferably, R^1 is (1) an C_1-C_{12} alkyl or cycloalkyl radical optionally substituted by 1-3 radicals of -OH, $-OR^3$, $-SR^3$, $-S(O)_2R^3$, $-NR^3R^4$, aryl, heteroaryl, cycloalkyl or heterocyclyl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl, cycloalkyl and heterocyclyl radicals are optionally substituted by 1-3 radicals of hydroxy, $-OR^3$, $-SR^3$, $-S(O)_2R^3$, $-NR^3R^4$, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_6 alkyl or $-CF_3$ radicals;

more preferably, R^1 is (1) an C_1-C_{12} alkyl or cycloalkyl radical optionally substituted by 1-2 radicals of -OH, $-OR^3$, $-NR^3R^4$, aryl, heteroaryl or cycloalkyl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl and cycloalkyl radicals are optionally substituted by 1-2 radicals of hydroxy, $-OR^3$, $-SR^3$, $-S(O)_2R^3$, $-NR^3R^4$, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, halo, C_1-C_6 alkyl or $-CF_3$ radicals;

more preferably, R^1 is (1) an C_1-C_{12} alkyl or cycloalkyl radical optionally substituted by 1-2 radicals of -OH, $-OR^3$, $-NR^3R^4$, aryl, heteroaryl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl and cycloalkyl radicals are optionally substituted by 1-2 radicals of hydroxy, $-OR^3$, $-SR^3$, $-S(O)_2R^3$, $-NR^3R^4$, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, halo, C_1-C_6 alkyl or $-CF_3$ radicals; and

most preferably, R^1 is (1) an C_5-C_{12} alkyl radical optionally substituted by 1-2 radicals of -OH, -OR^3 or -NR^3R^4; or (2) aryl or heteroaryl radicals optionally substituted by a hydroxy, -OR^3, -SR^3, -$S(O)_2R^3$, -NR^3R^4, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, halo, C_1-C_6 alkyl or -CF_3 radical; and

provided that the total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^1 is preferably 0-3, more preferably, 0-2, most preferably, 0-1;

wherein each R^3 is independently an alkyl, haloalkyl, aryl, heteroaryl, aryl-alkyl or heteroaryl-alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, alkoxy, alkylthiol, amino, alkanoylamino, alkylsulfonylamino, alkylsulfinyl, alkylsulfonyl, alkoxycarbonylamino, alkoxycarbonyl, cyano, halo, azido, alkyl, haloalkyl or haloalkoxy;

preferably, each R^3 is independently an C_1-C_8 alkyl, C_1-C_8 haloalkyl of 1-3 halo radicals, aryl, heteroaryl, aryl-C_1-C_4-alkyl or heteroaryl-C_1-C_4-alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, C_1-C_8 alkanoylamino, C_1-C_8 alkylsulfonylamino, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_1-C_8 alkoxycarbonylamino, C_1-C_8 alkoxycarbonyl, cyano, halo, azido, C_1-C_8 alkyl, C_1-C_8 haloalkyl of 1-3 halo radicals or C_1-C_8 haloalkoxy of 1-3 halo radicals;

more preferably, each R^3 is independently an C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals, aryl, heteroaryl, aryl-C_1-C_4-alkyl or heteroaryl-C_1-C_4-alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, C_1-C_4 alkanoylamino, C_1-C_4 alkylsulfonylamino, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals;

more preferably, each R^3 is independently an C_1-C_4 alkyl, -CF_3, aryl, heteroaryl, aryl-C_1-C_4-alkyl or heteroaryl-C_1-C_4-alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3;

more preferably, each R^3 is independently an C_1-C_4 alkyl, -CF_3, aryl, heteroaryl, aryl-C_1-C_2-alkyl or heteroaryl-C_1-C_2-alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3;

more preferably, each R^3 is independently an C_1-C_4 alkyl, -CF_3, aryl, heteroaryl, aryl-C_1-C_2-alkyl or heteroaryl-C_1-C_2-alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2

radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, methylsulfonylamino, C_1-C_2 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, halo, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$;

most preferably, each R^3 is independently an C_1-C_4 alkyl, $-CF_3$, aryl, heteroaryl, arylmethyl or heteroarylmethyl radical; and

each R^4 is independently a hydrogen or alkyl radical; preferably, each R^4 is independently a hydrogen or C_1-C_8 alkyl radical; more preferably, each R^4 is independently a hydrogen or C_1-C_4 alkyl radical; most preferably, each R^4 is independently a hydrogen or methyl radical; and

R^2 is a hydrogen or alkyl radical; preferably, R^2 is a hydrogen or C_1-C_4 alkyl radical; more preferably, R^2 is a hydrogen or methyl radical; and most preferably, R^2 is a hydrogen radical; and

V is $-CHR^{11}-$ or $-CHR^{11}-CHR^{12}-$; wherein R^{11} and R^{12} are each independently (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an alkyl, alkenyl or alkynyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, alkoxy, aryloxy, heteroaryloxy, alkylthiol, amino, alkanoylamino, alkylsulfonylamino,

alkoxycarbonylamino, alkoxycarbonyl, cyano, halo, azido, alkyl, haloalkyl or haloalkoxy;

preferably, R^{11} and R^{12} are each independently (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, amino, C_1-C_8 alkanoylamino, C_1-C_8 alkylsulfonylamino, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_1-C_8 alkoxycarbonylamino, C_1-C_8 alkoxycarbonyl, cyano, halo, azido, C_1-C_8 alkyl, C_1-C_8 haloalkyl of 1-3 halo radicals or C_1-C_8 haloalkoxy of 1-3 halo radicals;

more preferably, R^{11} and R^{12} are each independently (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3

radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, amino, C_1-C_4 alkanoylamino, C_1-C_4 alkylsulfonylamino, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals;

more preferably, R^{11} and R^{12} are each independently (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

when V is $-CHR^{11}-$, more preferably, R^{11} is (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$,

$-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

more preferably, R^{11} is (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, methylsulfonyl, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

more preferably, R^{11} is (1) a hydrogen, $-OR^{20}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, aryloxy,

heteroaryloxy, C_1-C_2 alkylthiol, halo, azido, C_1-C_2 alkyl, -CF_3 or -OCF_3 radicals; and

most preferably, R^{11} is (1) a hydrogen, -OR^{20}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-S$(O)_2$-R^{30}, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an -OR^{20}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-S$(O)_2$-R^{30}, aryl or heteroaryl radical;

alternatively, when V is -CHR^{11}-CHR^{12}-, more preferably, R^{11} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{12} is (1) a hydrogen, -OR^{20}, -SR^{21}, -C(O)R^{22}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-S$(O)_2$-R^{30}, -NR^{33}-S$(O)_2$-$NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an -OR^{20}, -SR^{21}, -C(O)R^{22}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-S$(O)_2$-R^{30}, -NR^{33}-S$(O)_2$-$NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals; or wherein R^{12} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{11} is (1) a hydrogen, -OR^{20}, -SR^{21}, -C(O)R^{22}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30},

$-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

more preferably, R^{11} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{12} is (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, methylsulfonyl, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; or wherein R^{12} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{11} is (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_8

alkyl, C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, methylsulfonyl, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

more preferably, R^{11} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{12} is (1) a hydrogen, $-OR^{20}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, aryloxy, heteroaryloxy, C_1-C_2 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals; or wherein R^{12} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{11} is (1) a hydrogen, $-OR^{20}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, aryloxy, heteroaryloxy, C_1-C_2

alkylthiol, halo, azido, C_1-C_2 alkyl, -CF_3 or -OCF_3 radicals; and

most preferably, R^{11} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{12} is (1) a hydrogen, -OR^{20}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-$S(O)_2$-R^{30}, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an -OR^{20}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-$S(O)_2$-R^{30}, aryl or heteroaryl radical; or wherein R^{12} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{11} is (1) a hydrogen, -OR^{20}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-$S(O)_2$-R^{30}, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an -OR^{20}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-$S(O)_2$-R^{30}, aryl or heteroaryl radical;

wherein each R^{20} is independently a hydrogen, -C(O)R^{22}, alkyl, alkenyl, cycloalkyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, alkanoyl, aroyl or heteroaroyl radical; wherein the alkyl and alkenyl radicals are optionally substituted by -C(O)R^{22}; and wherein the cycloalkyl, aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, alkoxy, alkylthiol, amino, alkanoylamino, alkylsulfonylamino, alkylsulfinyl, alkylsulfonyl, alkoxycarbonylamino, alkoxycarbonyl, cyano, halo, azido, alkyl, haloalkyl or haloalkoxy;

preferably, each R^{20} is independently a hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, cycloalkyl, aryl, heteroaryl, aryl-C_1-C_4-alkyl, heteroaryl-C_1-C_4-alkyl, C_1-C_8 alkanoyl, aroyl or heteroaroyl radical; wherein the alkyl and alkenyl radicals are optionally substituted by -C(O)R^{22}; and wherein the cycloalkyl, aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, C_1-C_8 alkanoylamino, C_1-C_8 alkylsulfonylamino, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_1-C_8 alkoxycarbonylamino, C_1-C_8 alkoxycarbonyl, cyano, halo, azido, C_1-C_8 alkyl, C_1-C_8 haloalkyl of 1-3 halo radicals or C_1-C_8 haloalkoxy of 1-3 halo radicals;

more preferably, each R^{20} is independently a hydrogen, C_1-C_4 alkyl, C_2-C_4 alkenyl, cycloalkyl, aryl, heteroaryl, aryl-C_1-C_4-alkyl, heteroaryl-C_1-C_4-alkyl, C_1-C_4 alkanoyl, aroyl or heteroaroyl radical; wherein the alkyl and alkenyl radicals are optionally substituted by -C(O)R^{22}; and wherein the cycloalkyl, aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, C_1-C_4 alkanoylamino, C_1-C_4 alkylsulfonylamino, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals;

more preferably, each R^{20} is independently a hydrogen, C_1-C_4 alkyl, C_2-C_4 alkenyl, cycloalkyl, aryl, heteroaryl, aryl-C_1-C_4-alkyl, heteroaryl-C_1-C_4-alkyl, C_1-C_4 alkanoyl, aroyl or heteroaroyl radical; wherein the alkyl and alkenyl radicals are optionally substituted by -C(O)R^{22}; and wherein the cycloalkyl, aryl and

heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals;

more preferably, each R^{20} is independently a hydrogen, C_1-C_4 alkyl-C(O)R^{22}, C_2-C_4 alkenyl, cycloalkyl, aryl, heteroaryl, aryl-C_1-C_2-alkyl, heteroaryl-C_1-C_2-alkyl or C_1-C_4 alkanoyl radical; and wherein the cycloalkyl, aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, halo, azido, C_1-C_2 alkyl, -CF_3 or -OCF_3 radicals; and

most preferably, each R^{20} is independently a hydrogen, C_2-C_4 alkenyl, cycloalkyl, aryl, heteroaryl, aryl-C_1-C_2-alkyl, heteroaryl-C_1-C_2-alkyl or C_1-C_4 alkanoyl radical;

wherein each R^{21} is independently an alkyl, alkyl-C(O)R^{22}, aryl, heteroaryl, aryl-alkyl or heteroaryl-alkyl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, alkoxy, alkylthiol, amino, alkanoylamino, alkylsulfonylamino, alkylsulfinyl, alkylsulfonyl, alkoxycarbonylamino, alkoxycarbonyl, cyano, halo, azido, alkyl, haloalkyl or haloalkoxy;

preferably, each R^{21} is independently an C_1-C_8 alkyl, C_1-C_8 alkyl-C(O)R^{22}, aryl, heteroaryl, aryl-C_1-C_4-alkyl or heteroaryl-C_1-C_4-alkyl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, C_1-C_8 alkanoylamino, C_1-C_8 alkylsulfonylamino, C_1-

C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_1-C_8 alkoxycarbonylamino, C_1-C_8 alkoxycarbonyl, cyano, halo, azido, C_1-C_8 alkyl, C_1-C_8 haloalkyl of 1-3 halo radicals or C_1-C_8 haloalkoxy of 1-3 halo radicals;

more preferably, each R^{21} is independently an C_1-C_4 alkyl, C_1-C_4 alkyl-C(O)R^{22}, aryl, heteroaryl, aryl-C_1-C_4-alkyl or heteroaryl-C_1-C_4-alkyl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, C_1-C_4 alkanoylamino, C_1-C_4 alkylsulfonylamino, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals;

more preferably, each R^{21} is independently an C_1-C_4 alkyl, C_1-C_4 alkyl-C(O)R^{22}, aryl, heteroaryl, aryl-C_1-C_4-alkyl or heteroaryl-C_1-C_4-alkyl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

most preferably, each R^{21} is independently an C_1-C_4 alkyl, C_1-C_4 alkyl-C(O)R^{22}, aryl, heteroaryl, aryl-C_1-C_2-alkyl or heteroaryl-C_1-C_2-alkyl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4

alkylthiol, halo, azido, C_1-C_2 alkyl, -CF_3 or -OCF_3 radicals;

wherein each R^{22} is independently a hydroxy, alkoxy, aryloxy, aryl-alkoxy, heteroaryloxy, heteroaryl-alkoxy or -$NR^{23}R^{24}$ radical; preferably, each R^{22} is independently a hydroxy, C_1-C_8 alkoxy, aryloxy, aryl-C_1-C_4-alkoxy, heteroaryloxy, heteroaryl-C_1-C_4-alkoxy or -$NR^{23}R^{24}$ radical; more preferably, each R^{22} is independently a hydroxy, C_1-C_4 alkoxy, aryloxy, aryl-C_1-C_2-alkoxy, heteroaryloxy, heteroaryl-C_1-C_2-alkoxy or -$NR^{23}R^{24}$ radical; and most preferably, each R^{22} is independently a hydroxy or -$NR^{23}R^{24}$ radical;

wherein R^{23} is a hydrogen, alkyl, aryl, aryl-alkyl, heteroaryl or heteroaryl-alkyl radical; preferably, R^{23} is a hydrogen, C_1-C_8 alkyl, aryl, aryl-C_1-C_4-alkyl, heteroaryl or heteroaryl-C_1-C_4-alkyl radical; more preferably, R^{23} is a hydrogen, C_1-C_4 alkyl, aryl, aryl-C_1-C_2-alkyl, heteroaryl or heteroaryl-C_1-C_2-alkyl radical; and most preferably, R^{23} is a hydrogen, C_1-C_2 alkyl, aryl, aryl-C_1-C_2-alkyl, heteroaryl or heteroaryl-C_1-C_2-alkyl radical; and

R^{24} is a hydrogen or alkyl radical; preferably, R^{24} is a hydrogen or C_1-C_8 alkyl radical; more preferably, R^{24} is a hydrogen or C_1-C_4 alkyl radical; and most preferably, R^{24} is a hydrogen or C_1-C_2 alkyl radical; or

-$NR^{23}R^{24}$ represents a heterocyclyl or heteroaryl radical; preferably, -$NR^{23}R^{24}$ represents a heteroaryl radical; and

wherein the heterocyclyl, aryl and heteroaryl radicals of R^{22}, R^{23} and $-NR^{23}R^{24}$ are optionally substituted by 1-3 radicals of hydroxy, alkoxy, alkylthiol, amino, alkanoyl-amino, alkylsulfonylamino, alkylsulfinyl, alkylsulfonyl, alkoxycarbonylamino, alkoxycarbonyl, cyano, halo, azido, alkyl, haloalkyl or haloalkoxy; preferably, 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, C_1-C_8 alkanoylamino, C_1-C_8 alkylsulfonylamino, C_1-C_4 alkyl-sulfinyl, C_1-C_4 alkylsulfonyl, C_1-C_8 alkoxycarbonylamino, C_1-C_8 alkoxycarbonyl, cyano, halo, azido, C_1-C_8 alkyl, C_1-C_8 haloalkyl of 1-3 halo radicals or C_1-C_8 haloalkoxy of 1-3 halo radicals; more preferably, 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, C_1-C_4 alkanoylamino, C_1-C_4 alkylsulfonylamino, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_1-C_4 alkoxycarbonyl-amino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals; more preferably, 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; more preferably, 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; and most preferably, 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals;

W-N represents $-C(O)-N$, $-C(O)-CR^{15}R^{16}-N$, $-CR^{15}R^{16}-N$ or $-CR^{17}R^{18}-CR^{15}R^{16}-N$; preferably, W-N represents $-C(O)-CR^{15}R^{16}-N$, $-CR^{15}R^{16}-N$ or $-CR^{17}R^{18}-CR^{15}R^{16}-N$; more preferably,

when V is $-CHR^{11}-CHR^{12}-$, W-N represents -C(O)-N or $-CR^{15}R^{16}-N$; preferably, $-CR^{15}R^{16}-N$; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-3; preferably, 0-2; and more preferably, 0-1;

wherein R^{15} and R^{16} are each independently (1) a hydrogen, $-C(O)R^{22}$, aryl or heteroaryl radical; or (2) an alkyl, alkenyl or alkynyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, alkoxy, alkylthiol, amino, alkanoylamino, alkylsulfonylamino, alkylsulfinyl, alkylsulfonyl, alkoxycarbonylamino, alkoxycarbonyl, cyano, halo, azido, alkyl, haloalkyl or haloalkoxy;

preferably, R^{15} and R^{16} are each independently (1) a hydrogen, $-C(O)R^{22}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, C_1-C_8 alkanoylamino, C_1-C_8 alkylsulfonylamino, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_1-C_8 alkoxycarbonylamino, C_1-C_8 alkoxycarbonyl, cyano, halo, azido, C_1-C_8 alkyl, C_1-C_8 haloalkyl of 1-3 halo radicals or C_1-C_8 haloalkoxy of 1-3 halo radicals;

more preferably, R^{15} and R^{16} are each independently (1) a hydrogen, $-C(O)R^{22}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical

optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, C_1-C_4 alkanoylamino, C_1-C_4 alkylsulfonylamino, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals;

more preferably, R^{16} is a hydrogen radical; and R^{15} is (1) a hydrogen, $-C(O)R^{22}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

more preferably, R^{15} is (1) a hydrogen, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl radical optionally substituted with an $-OR^{20}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, C_1-C_4 alkoxycarbonyl-amino, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

most preferably, R^{15} is (1) a hydrogen, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl radical

optionally substituted with an aryl or heteroaryl radical; and

wherein R^{17} and R^{18} are each independently (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an alkyl, alkenyl or alkynyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, alkoxy, alkylthiol, amino, alkanoylamino, alkylsulfonylamino, alkylsulfinyl, alkylsulfonyl, alkoxycarbonylamino, alkoxycarbonyl, cyano, halo, azido, alkyl, haloalkyl or haloalkoxy;

preferably, R^{17} and R^{18} are each independently (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, C_1-C_8 alkanoylamino, C_1-C_8 alkylsulfonylamino, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_1-C_8 alkoxycarbonylamino, C_1-C_8 alkoxycarbonyl, cyano, halo, azido, C_1-C_8 alkyl, C_1-C_8

haloalkyl of 1-3 halo radicals or C_1-C_8 haloalkoxy of 1-3 halo radicals;

more preferably, R^{17} and R^{18} are each independently (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, C_1-C_4 alkanoylamino, C_1-C_4 alkylsulfonylamino, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals;

more preferably, R^{18} is a hydrogen radical, and R^{17} is (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino,

methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

more preferably, R^{17} is (1) a hydrogen, $-OR^{20}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl radical optionally substituted with an $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

most preferably, R^{17} is a hydrogen, hydroxy or C_1-C_4 alkyl radical; and

alternatively, one of $-CR^{15}R^{16}-$ or $-CR^{17}R^{18}-$ represent a cycloalkylene or heterocyclylene radical; and

X is O, Y is CR^9 and Z is N; or
X is S, Y is CR^9 and Z is CR^{10}; or
X is O, Y is CR^9 and Z is N; or
X is S, Y is CR^9 and Z is CR^{10}; or
Y is O, X is CR^8 and Z is CR^{10}; or
Y is S, X is CR^8 and Z is CR^{10}; or
Z is O, X is N and Y is CR^9; or
Z is S, X is CR^8 and Y is CR^9; or
Z is O, X is N and Y is CR^9; or
Z is S, X is CR^8 and Y is CR^9;

preferably, when W-N represents $-CR^{15}R^{16}-N$ or $-CR^{17}R^{18}-CR^{15}R^{16}-N$, and X is S and Z is CR^{10}, then at least one of R^{11}, R^{12}, R^{15}, R^{16}, R^{17} or R^{18} is other than a hydrogen radical; more preferably, when X is S and Z is CR^{10} or when Z is S and X is CR^{8}, then at least one of R^{11}, R^{12}, R^{15}, R^{16}, R^{17} or R^{18} is other than a hydrogen radical; more preferably, at least one of R^{11}, R^{12}, R^{15}, R^{16}, R^{17} or R^{18} is other than a hydrogen radical;

wherein R^{8}, R^{9} and R^{10} are each independently -B-A, provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^{8}, R^{9} and R^{10} is 0-3; preferably 0-2; and more preferably, 0-1

preferably, R^{8} is a radical of hydrogen, halo, C_1-C_2 alkoxy, amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, amidino, amido, carboxy, or C_1-C_4 alkyl optionally substituted by amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, 1-3 halo radicals, amidino, amido or carboxy radical; more preferably, R^{8} is a radical of hydrogen, halo, C_1-C_2 alkoxy, $-CF_3$ or C_1-C_4 alkyl optionally substituted by hydroxy or C_1-C_2 alkoxy radical; and most preferably, R^{8} is a radical of hydrogen, halo, C_1-C_2 alkoxy, $-CF_3$ or methyl; and

when V is $-CHR^{11}-$ and Z is CR^{10}, preferably, R^{10} is independently -B-A when R^{11} is a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical; and when R^{11} is other than a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl

radical, then R^{10} is independently a radical of hydrogen, halo, C_1-C_2 alkoxy, amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, amidino, amido, carboxy, or C_1-C_4 alkyl optionally substituted by amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, 1-3 halo radicals, amidino, amido or carboxy radical;

more preferably, R^{10} is independently -B-A when R^{11} is a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical; and when R^{11} is other than a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical, then R^{10} is independently a radical of hydrogen, halo, C_1-C_2 alkoxy, $-CF_3$ or C_1-C_4 alkyl optionally substituted by hydroxy or C_1-C_2 alkoxy radical;

more preferably, R^{10} is independently -B-A when R^{11} is a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical; and when R^{11} is other than a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical, then R^{10} is independently a radical of hydrogen, halo, C_1-C_2 alkoxy, $-CF_3$ or methyl radical;

alternatively, when V is $-CHR^{11}-CHR^{12}-$ and Z is CR^{10}, preferably, R^{10} is independently -B-A when R^{11} and R^{12} are each independently a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical; and when R^{11} or R^{12} is independently other than a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical, then R^{10} is independently a radical of hydrogen, halo, C_1-C_2 alkoxy, amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, amidino, amido, carboxy, or C_1-C_4 alkyl optionally substituted by

amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, 1-3 halo radicals, amidino, amido or carboxy radical;

more preferably, R^{10} is independently -B-A when R^{11} and R^{12} are each independently a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical; and when R^{11} or R^{12} is independently other than a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical, then R^{10} is independently a radical of hydrogen, halo, C_1-C_2 alkoxy, $-CF_3$ or C_1-C_4 alkyl optionally substituted by hydroxy or C_1-C_2 alkoxy radical;

more preferably, R^{10} is independently -B-A when R^{11} and R^{12} are each independently a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical; and when R^{11} or R^{12} is independently other than a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical, then R^{10} is independently a radical of hydrogen, halo, C_1-C_2 alkoxy, $-CF_3$ or methyl;

wherein each B is independently a (1) bond; (2) alkyl, alkenyl or alkynyl radical optionally substituted by (a) 1-3 radicals of amino, alkylamino, dialkylamino, alkanoylamino, alkoxycarbonylamino, alkylsulfonylamino, hydroxy, alkoxy, alkylthio, cyano or halo, and/or (b) 1-2 radicals of heterocyclyl, aryl or heteroaryl optionally substituted by 1-3 radicals of amino, alkylamino, dialkylamino, alkanoylamino, alkoxycarbonylamino, alkylsulfonylamino, hydroxy, alkoxy, alkylthio, cyano, halo, alkyl, haloalkyl or haloalkoxy; (3) heterocyclyl radical optionally substituted by 1-3 radicals of amino, alkylamino, dialkylamino, alkanoylamino, alkoxycarbonylamino,

alkylsulfonylamino, hydroxy, alkoxy, alkylthio, cyano, alkyl, haloalkyl or haloalkoxy; or (4) aryl or heteroaryl radical optionally substituted by 1-3 radicals of amino, alkylamino, dialkylamino, alkanoylamino, alkoxycarbonylamino, alkylsulfonylamino, hydroxy, alkoxy, alkylthio, cyano, halo, alkyl, haloalkyl or haloalkoxy;

preferably, each B is independently a (1) bond; (2) C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted by (a) 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, halo, and/or (b) 1-2 radicals of heterocyclyl, aryl or heteroaryl optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals; (3) heterocyclyl radical optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals; or (4) aryl or heteroaryl radical optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, halo, C_1-C_4 alkyl, C_1-C_8 haloalkyl of 1-3 halo radicals or C_1-C_8 haloalkoxy of 1-3 halo radicals;

more preferably, each B is independently a (1) bond; (2) C_1-C_8 alkyl radical optionally substituted by (a) a radical of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio or cyano and/or (b) 1-3 halo radicals, and/or (c) 1-2 radicals of heterocyclyl, aryl or heteroaryl optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals; (3) heterocyclyl radical; or (4) aryl or heteroaryl radical optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals;

more preferably, each B is independently a (1) bond; (2) C_1-C_8 alkyl radical optionally substituted by (a) a radical of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, and/or (b) 1-3 halo radicals, and/or (c) 1-2 radicals of heterocyclyl, aryl or heteroaryl optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, halo, C_1-C_4 alkyl,

-CF_3 or -OCF_3 radicals; (3) heterocyclyl radical; or (4) aryl or heteroaryl radical optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonyl-amino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals;

more preferably, each B is independently a (1) bond; (2) C_1-C_4 alkyl radical optionally substituted by (a) a radical of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, hydroxy or C_1-C_2 alkoxy and/or (b) 1-2 halo radicals, and/or (c) a radical of heterocyclyl, aryl or heteroaryl optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_2 alkylsulfonylamino, hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthio, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals; (3) heterocyclyl radical; or (4) aryl or heteroaryl radical optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_2 alkylsulfonylamino, hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthio, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals;

more preferably, each B is independently a (1) bond; (2) C_1-C_4 alkyl radical; or (3) aryl or heteroaryl radical optionally substituted by a radical of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_2 alkylsulfonylamino, hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthio, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals; and most preferably, each

B is independently a bond, C_1-C_4 alkyl, aryl or heteroaryl radical; and

each A is independently a (1) hydrogen radical; (2) halo, cyano or nitro radical; (3) $-C(O)-R^{30}$, $-C(O)-OR^{31}$, $-C(O)-NR^{32}R^{31}$ or $-C(NR^{32})-NR^{32}R^{31}$ radical; (4) $-OR^{31}$, $-O-C(O)-R^{31}$, $-O-C(O)-NR^{32}R^{31}$ or $-O-C(O)-NR^{33}-S(O)_2-R^{30}$ radical; (5) $-SR^{31}$, $-S(O)-R^{30}$, $-S(O)_2-R^{30}$, $-S(O)_2-NR^{32}R^{31}$, $-S(O)_2-NR^{33}-C(O)-R^{31}$, $-S(O)_2-NR^{33}-C(O)-OR^{30}$ or $-S(O)_2-NR^{33}-C(O)-NR^{32}R^{31}$ radical; or (6) $-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(NR^{32})-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$ or $-NR^{33}-S(O)_2-NR^{32}R^{31}$ radical;

preferably, each A is independently a (1) hydrogen radical; (2) halo, cyano or nitro radical; (3) $-C(O)-R^{30}$, $-C(O)-OR^{31}$, $-C(O)-NR^{32}R^{31}$ or $-C(NR^{32})-NR^{32}R^{31}$ radical; (4) $-OR^{31}$, $-O-C(O)-R^{31}$ or $-O-C(O)-NR^{32}R^{31}$ radical; (5) $-SR^{31}$, $-S(O)-R^{30}$, $-S(O)_2-R^{30}$ or $-S(O)_2-NR^{32}R^{31}$ radical; or (6) $-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(NR^{32})-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$ or $-NR^{33}-S(O)_2-NR^{32}R^{31}$ radical;

more preferably, each A is independently a (1) hydrogen radical; (2) halo radical; (3) $-C(O)-R^{30}$, $-C(O)-OR^{31}$, $-C(O)-NR^{32}R^{31}$ or $-C(NR^{32})-NR^{32}R^{31}$ radical; (4) $-OR^{31}$ radical; (5) $-SR^{31}$, $-S(O)_2-R^{30}$ or $-S(O)_2-NR^{32}R^{31}$ radical; or (6) $-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$ or $-NR^{33}-S(O)_2-NR^{32}R^{31}$ radical;

more preferably, each A is independently a (1) hydrogen radical; (2) halo radical; (3) $-C(O)-R^{30}$, $-C(O)-OR^{31}$, $-C(O)-NR^{32}R^{31}$ or $-C(NR^{32})-NR^{32}R^{31}$ radical; (4) $-OR^{31}$ radical; (5) $-SR^{31}$, $-S(O)_2-R^{30}$ or $-S(O)_2-NR^{32}R^{31}$ radical; or (6) $-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$ or $-NR^{33}-S(O)_2-R^{30}$ radical; and most preferably, each A is independently a hydrogen, halo, $-C(O)-R^{30}$, $-C(O)-OR^{31}$ or $-C(O)-NR^{32}R^{31}$ radical;

wherein each R^{30} is independently

(1) alkyl, alkenyl or alkynyl radicals optionally substituted by 1-3 radicals of $-CO_2R^{34}$, amino, alkylamino, dialkylamino, alkanoylamino, alkoxycarbonylamino, N-(alkoxycarbonyl)-N-(alkyl)amino, aminocarbonylamino, alkylsulfonylamino, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, hydroxy, cyano, halo or aralkoxy, arylalkylthio, arylalkylsulfonyl, cycloalkyl, heterocyclyl, aryl or heteroaryl radicals, wherein the cycloalkyl, heterocyclyl, aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of amino, alkylamino, dialkylamino, alkanoylamino, alkoxycarbonyl-amino, alkylsulfonylamino, alkanoyl, alkoxycarbonyl, hydroxy, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, cyano, halo, alkyl, haloalkyl or haloalkoxy;

(2) cycloalkyl or heterocyclyl radical optionally substituted by 1-3 radicals of amino, alkylamino, dialkylamino, alkanoylamino, alkoxycarbonylamino, alkylsulfonylamino, alkoxycarbonyl, hydroxy, alkoxy, alkylthio, cyano, alkyl, haloalkyl or haloalkoxy; or

(3) aryl or heteroaryl radicals optionally substituted by 1-3 radicals of amino, alkylamino, dialkylamino, alkanoylamino, alkoxycarbonylamino, alkylsulfonylamino, alkoxycarbonyl, hydroxy, alkoxy, alkylthio, cyano, halo, azido, alkyl, haloalkyl or haloalkoxy;

preferably, each R^{30} is independently

(1) C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radicals optionally substituted by 1-3 radicals of -CO_2R^{34}, amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoyl-amino, (C_1-C_4 alkoxy)carbonylamino, N-((C_1-C_4 alkoxy) carbonyl)-N-(C_1-C_4 alkyl)amino, aminocarbonylamino, C_1-C_4 alkylsulfonylamino, C_1-C_4 alkoxy, C_1-C_4 alkylthio, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, hydroxy, cyano, halo or aryl-C_1-C_4-alkoxy, aryl-C_1-C_4-alkylthio, aryl-C_1-C_4-alkylsulfonyl, C_3-C_8 cycloalkyl, heterocyclyl, aryl or heteroaryl radicals, wherein the cycloalkyl, aryl, heterocyclyl and heteroaryl radicals are optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy) carbonylamino, C_1-C_4 alkylsulfonylamino, C_1-C_5 alkanoyl, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, cyano, halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals;

(2) cycloalkyl or heterocyclyl radical optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals; or

(3) aryl or heteroaryl radicals optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, halo, azido, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals;

more preferably, each R^{30} is independently (1) C_1-C_6 alkyl radicals optionally substituted by 1-3 radicals of -CO_2R^{34}, amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonyl-amino, N-((C_1-C_4 alkoxy)carbonyl)-N-(C_1-C_4 alkyl)amino, aminocarbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, cyano, halo or aryl-C_1-C_4-alkoxy, aryl-C_1-C_4-alkylthio, aryl-C_1-C_4-alkylsulfonyl, C_3-C_8 cycloalkyl, heterocyclyl, aryl or heteroaryl radicals, wherein the cycloalkyl, heterocyclyl, aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, C_1-C_5 alkanoyl, (C_1-C_4 alkoxy)carbonyl, C_1-C_4 alkoxy, C_1-C_4 alkylthio, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, hydroxy, cyano, halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals;

(2) cycloalkyl or heterocyclyl radical optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals; or

(3) aryl or heteroaryl radicals optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio,

cyano, halo, azido, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals;

more preferably, each R^{30} is independently (1) C_1-C_6 alkyl radical optionally substituted by 1-3 radicals of $-CO_2R^{34}$, amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonyl-amino, N-((C_1-C_4 alkoxy)carbonyl)-N-(C_1-C_4 alkyl)amino, aminocarbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, cyano, halo or aryl-C_1-C_4-alkoxy, aryl-C_1-C_4-alkylthio, aryl-C_1-C_4-alkylsulfonyl, C_3-C_8 cycloalkyl, heterocyclyl, aryl or heteroaryl radicals, wherein the cycloalkyl, heterocyclyl, aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, C_1-C_5 alkanoyl, (C_1-C_4 alkoxy)carbonyl, C_1-C_4 alkoxy, C_1-C_4 alkylthio, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, hydroxy, cyano, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

(2) cycloalkyl or heterocyclyl radical optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, C_1-C_4 alkyl, C_1-C_2 haloalkyl of 1-3 halo radicals or $-OCF_3$; or

(3) aryl or heteroaryl radicals optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, (C_1-C_4

alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals;

more preferably, each R^{30} is independently (1) -CF_3 or C_1-C_4 alkyl radical optionally substituted by 1-2 radicals of -CO_2R^{34}, amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonyl-amino, N-((C_1-C_4 alkoxy)carbonyl)-N-(C_1-C_4 alkyl)amino, hydroxy, C_1-C_4 alkoxy or aryl-C_1-C_2-alkoxy, heterocyclyl, aryl or heteroaryl radicals, wherein the heterocyclyl, aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonyl-amino, C_1-C_5 alkanoyl, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals;
(2) cycloalkyl or heterocyclyl radical optionally substituted by 1-2 radicals of (C_1-C_4 alkoxy)carbonyl, hydroxy or C_1-C_4 alkyl; or
(3) aryl or heteroaryl radicals optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals;

more preferably, each R^{30} is independently (1) heterocyclyl radical optionally substituted by 1-2 radicals of (C_1-C_4 alkoxy)carbonyl, hydroxy or C_1-C_4 alkyl; or (2) heteroaryl radicals optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals; and most preferably, each R^{30} is independently a heterocyclyl radical optionally substituted by C_1-C_4 alkyl;

each R^{31} is independently hydrogen radical or R^{30}; alternatively, more preferably, each R^{31} is independently hydrogen radical or (1) $-CF_3$ or C_1-C_4 alkyl radical optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy or aryl-C_1-C_2-alkoxy, aryl or heteroaryl radicals, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy) carbonylamino, C_1-C_5 alkanoyl, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; (2) cycloalkyl radical optionally substituted by 1-2 radicals of hydroxy or C_1-C_4 alkyl; or (3) aryl or heteroaryl radicals optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl) amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

most preferably, each R^{31} is independently hydrogen radical or (1) C_1-C_4 alkyl radical optionally substituted by 1-2 radicals of aryl or heteroaryl radicals, wherein the aryl and heteroaryl radicals are optionally substituted by a hydroxy, C_1-C_4 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radical; or (2) cycloalkyl radical optionally substituted by 1-2 radicals of hydroxy or C_1-C_4 alkyl; or (3) aryl or heteroaryl radicals optionally substituted by a hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

wherein each R^{32} is independently (1) hydrogen radicals; (2) alkyl, alkenyl or alkynyl radicals optionally substituted by 1-3 radicals of amino, alkylamino, dialkylamino, hydroxy, alkoxy, alkylthio, cyano or halo; or (3) aryl, heteroaryl, arylalkyl, heteroarylalkyl, heterocyclyl, heterocyclylalkyl, cycloalkyl or

cycloalkylalkyl radicals optionally substituted by 1-3 radicals of amino, alkylamino, dialkylamino, hydroxy, alkoxy, alkylthio, cyano, alkyl, haloalkyl or haloalkoxy; preferably, each R^{32} is independently (1) hydrogen radicals; (2) C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radicals optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4-alkyl)amino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano or halo; or (3) aryl, heteroaryl, aryl-C_1-C_4-alkyl, heteroaryl-C_1-C_4-alkyl, heterocyclyl, heterocyclyl-C_1-C_4-alkyl, C_3-C_8 cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl radicals optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4-alkyl)amino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals; and most preferably, each R^{32} is independently a hydrogen or C_1-C_4 alkyl radical;

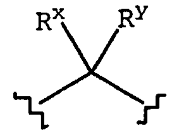
each R^{33} is independently (1) hydrogen radical; (2) alkyl radical optionally substituted by a radical of heterocyclyl, aryl or heteroaryl which is optionally substituted by 1-3 radicals of amino, alkylamino, dialkylamino, alkanoylamino, alkoxycarbonylamino, alkylsulfonylamino, hydroxy, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, cyano, halo, alkyl, haloalkyl or haloalkoxy; or (3) heterocyclyl, aryl or heteroaryl radicals optionally substituted by 1-3 radicals of amino, alkylamino, dialkylamino, alkanoylamino, alkoxycarbonylamino, alkylsulfonylamino, hydroxy, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, cyano, halo, alkyl, haloalkyl or haloalkoxy; and preferably, each R^{33} is independently (1) hydrogen radical; (2) C_1-C_4 alkyl radical optionally substituted by a radical of heterocyclyl, aryl or heteroaryl which is optionally

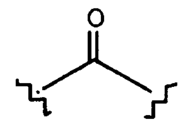
substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy) carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, cyano, halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals; or (3) heterocyclyl, aryl or heteroaryl radicals optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoyl-amino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonyl-amino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, cyano, halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals; more preferably, each R^{33} is independently a hydrogen or C_1-C_4 alkyl radical; and most preferably, each R^{33} is independently a hydrogen or methyl radical; and

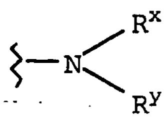
each R^{34} is independently hydrogen, alkyl, heteroaryl, aryl, arylalkyl or heteroarylalkyl radicals, wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of cyano, halo, alkyl, amino, alkylamino, dialkylamino, alkanoylamino, alkoxycarbonylamino, alkylsulfonylamino, hydroxy, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, haloalkyl or haloalkoxy; preferably, each R^{34} is independently hydrogen or C_1-C_4 alkyl, aryl, heteroaryl, aryl-C_1-C_4-alkyl or heteroaryl-C_1-C_4-alkyl radicals, wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, C_1-C_4 alkylsulfinyl, C_1-C_4

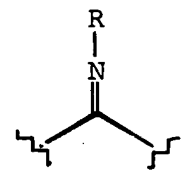
alkylsulfonyl, cyano, halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals; and most preferably, each R^{34} is independently a hydrogen or C_1-C_4 alkyl radical.

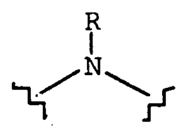
The symbols used above have the following meanings:

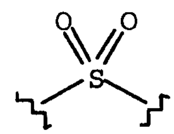
$-CR^xR^y-$ = 

$-C(O)-$ = 

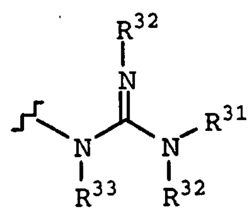
$-NR^xR^y$ = 

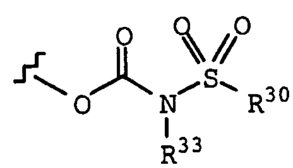
$-C(NR)-$ = 

$-NR-$ = 

$-S(O)_2-$ = 

For example:

$-NR^{33}-C(NR^{32})-NR^{32}R^{31}$ = 

$-O-C(O)-NR^{33}-S(O)_2-R^{30}$ = 

The compounds of this invention have in general several asymmetric centers and are depicted in the form of racemic mixtures. This invention is intended to encompass racemic mixtures, partially racemic mixtures and separate enantiomers and diasteromers. Preferably, the absolute configuration of the hydroxamic acid group is (R).

Compounds of interest include the following:

cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-benzyl-N-methylaminocarbonyl)-6-(N-hydroxyaminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine;

cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-phenyl-6-(N-hydroxyaminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2,-c]-pyridine;

cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(methoxy carbonyl)-6-(N-hydroxyaminocarbonyl)-4,5,6,7-tetrahydro thieno-[3,2-c]-pyridine;

cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(ethoxy carbonyl)-6-(N-hydroxyaminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine;

cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(2-pyridyl)-6-(N-hydroxyaminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine;

cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(3-pyridyl)-6-(N-hydroxyaminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine;

cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(4-morpholino carbonyl)-6-(N-hydroxyaminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine;

cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(phenoxy carbonyl)-6-(N-hydroxyaminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine;

cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-benzylaminocarbonyl)-6-(N-hydroxyaminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine;

cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-(3-phenylpropyl)aminocarbonyl)-6-(N-hydroxyaminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine;

cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-phenethyl-N-methylaminocarbonyl)-6-(N-hydroxyaminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine;

cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-benzyl-N-ethylaminocarbonyl)-6-(N-hydroxyaminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine;

cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-(4,4-dimethylpentyl)aminocarbonyl)-6-(N-hydroxyaminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine;

cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-(4,4-diphenylbutyl)aminocarbonyl)-6-(N-hydroxyaminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine;

cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-methyl-N-phenylaminocarbonyl)-6-(N-hydroxyaminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine;

trans-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-methyl-N-phenylaminocarbonyl)-6-(N-hydroxyaminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine;

cis 7-benzylcarbamoyloxy-5-(4-methoxyphenylsulfony)-4,5,6,7-tetrahydro-thieno[3,2-c]pyridinyl-6-hydroxamic acid;

cis 7-phenylcarbamoyloxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[3,2-c]pyridinyl-6-hydroxamic acid;

cis 7-methylcarbamoyloxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[3,2-c]pyridinyl-6-hydroxamic acid;

cis 7-isopropylcarbamoyloxy-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydro-thieno[3,2-c]pyridinyl-6-hydroxamic acid;

cis 7-(4-phenoxyphenyl)carbamoyloxy-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydro-thieno[3,2-c]pyridinyl-6-hydroxamic acid;

cis 7-(S)-(N-methyl-N-benzylcarbamoyloxy)-5-(4-methoxy phenylsulfonyl)-4,5,6,7-tetrahydro-thieno[3,2-c]pyridinyl-6-hydroxamic acid;

cis 7-(4-methoxyphenyl)carbamoyloxy-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydro-thieno[3,2-c]pyridinyl-6-hydroxamic acid;

cis 7-phenethylcarbamoyloxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[3,2-c]pyridinyl-6-hydroxamic acid;

4-benzyl-8-cis-hydroxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid;

4-cis-Benzyl-8-cis-hydroxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid;

4-trans-benzyl-8-(hydroxy)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid;

4-trans-benzyl-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid;

4-trans-benzyl-6-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[2,3,-c]pyridine-5-hydroxamic acid;

4-cis-hydroxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid;

4-trans-hydroxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid;

4-cis-vinyl-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid;

4-cis-hydroxymethyl-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid;

4-trans-benzyl-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid;

6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-hydroxamic acid;

4-oxo-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-hydroxamic acid;

4-cis-hydroxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-hydroxamic acid;

4-cis-methoxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-hydroxamic acid;

5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-trans-hydroxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-methyl-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

5-(4-methoxyphenylsulfonyl)-2-carboxy-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-carboxy-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

5-(4-methoxyphenylsulfonyl)-2-(methoxycarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(methoxycarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(ethoxycarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-pyrid-2-yl-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-pyrid-3-yl-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-phenyl-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-phenylaminocarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-(phenylmethyl)aminocarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-phenylmethyl-N-methylaminocarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-(3-phenylpropyl)aminocarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-(4,4-diphenylbutyl)aminocarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-(3,3-dimethylbutyl)aminocarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(aminocarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-methylaminocarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N,N-dimethylaminocarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(morpholinocarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(4-methylpiperazin-1-ylcarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-(pyridylmethyl)aminocarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

4-benzyl-8-cis-hydroxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid;

4-cis-benzyl-8-cis-hydroxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid;

4-trans-benzyl-8-hydroxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid;

4-trans-benzyl-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid;

4-trans-benzyl-6-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[2,3,-c]pyridine-5-hydroxamic acid;

7-cis-(aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-(N-methylaminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-(N-prop-2-ylaminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-(N-cyclohexylaminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-(N-phenylaminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-(N-(4-methoxyphenyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-(N-(4-phenoxyphenyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-(N-(2-biphenyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-(N-(phenylmethyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-(N-(1(S)-phenylethyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-(N-(2-phenylethyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-(N-(3-methoxyphenyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-(N-(2-methoxyphenyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-(N-(2-chlorophenyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-(N-(3-chlorophenyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-(N-(4-chlorophenyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-(N-(4-fluorophenyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-(N-(4-cyanophenyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-(N-(4-butoxycarbonylphenyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-(N-(4-tolyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-(N-(3-tolyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

7-cis-(N-(1-naphthyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid;

5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thiazolo[4,5-c]pyridinyl-6-hydroxamic acid;

2-(phenylsulfonylamino)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothiazolo[4,5-c]pyridinyl-6-hydroxamic acid;

7-hydroxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothiazolo[4,5-c]pyridinyl-6-hydroxamic acid;

7-(phenylcarbamoyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothiazolo[4,5-c]pyridinyl-6-hydroxamic acid;

2-(acetylamino)-7-hydroxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothiazolo[4,5-c]pyridinyl-6-hydroxamic acid;

2-(methylcarbamoylamino)-7-(4-fluorophenyl)carbamoyloxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothiazolo[4,5-c]pyridinyl-6-hydroxamic acid;

5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridinyl-6-hydroxamic acid;

2-methyl-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridinyl-6-hydroxamic acid;

7-hydroxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridinyl-6-hydroxamic acid;

7-(phenylcarbamoyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridinyl-6-hydroxamic acid;

7-benzyl-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thiazolo[5,4-c]pyridinyl-6-hydroxamic acid;

2-benzoylamino-7-hydroxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridinyl-6-hydroxamic acid;

2-methyl-7-(phenylcarbamoyloxy)-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrothiazolo[5,4-c]pyridinyl-6-hydroxamic acid;

5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrofuro[3,2-c]pyridinyl-6-hydroxamic acid;

2-(ethoxycarbonyl)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrofuro[3,2-c]pyridinyl-6-hydroxamic acid;

7-hydroxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrofuro[3,2-c]pyridinyl-6-hydroxamic acid;

7-(phenylcarbamoyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrofuro[3,2-c]pyridinyl-6-hydroxamic acid;

2-methyl-7-(phenylcarbamoyloxy)-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrofuro[3,2-c]pyridinyl-6-hydroxamic acid;

5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrofuro[3,4-c]pyridinyl-6-hydroxamic acid;

7-(phenylcarbamoyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrofuro[3,4-c]pyridinyl-6-hydroxamic acid;

7-hydroxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrofuro[3,4-c]pyridinyl-6-hydroxamic acid;

5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno [3,4-c]pyridinyl-6-hydroxamic acid;

7-(phenylcarbamoyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,4-c]pyridinyl-6-hydroxamic acid; and

7-hydroxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,4-c]pyridinyl-6-hydroxamic acid.

As utilized herein, the following terms shall have the following meanings:

"Alkyl", alone or in combination, means a straight-chain or branched-chain alkyl radical containing preferably 1-15 carbon atoms (C_1-C_{15}), more preferably 1-8 carbon atoms (C_1-C_8), even more preferably 1-6 carbon atoms (C_1-C_6), yet more preferably 1-4 carbon atoms (C_1-C_4), still more preferably 1-3 carbon atoms (C_1-C_3), and most preferably 1-2 carbon atoms (C_1-C_2). Examples of such radicals include methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, pentyl, iso-amyl, hexyl, octyl and the like.

"Alkenyl", alone or in combination, means a straight-chain or branched-chain hydrocarbon radical having one or more double bonds, preferably 1-2 double bonds and more preferably one double bond, and containing preferably 2-15 carbon atoms (C_2-C_{15}), more preferably 2-8 carbon atoms (C_2-C_8), even more preferably 2-6 carbon atoms (C_2-C_6), yet more preferably 2-4 carbon atoms (C_2-C_4), and still more preferably 2-3 carbon atoms (C_2-C_3). Examples of such alkenyl radicals include ethenyl, propenyl, 2-methylpropenyl, 1,4-butadienyl and the like.

"Alkynyl", alone or in combination, means a straight-chain or branched chain hydrocarbon radical having one or more triple bonds, preferably 1-2 triple bonds and more preferably one triple bond, and containing preferably 2-15 carbon atoms (C_2-C_{15}), more preferably 2-8 carbon atoms (C_2-C_8), even more preferably 2-6 carbon atoms (C_2-C_6), yet more preferably 2-4 carbon atoms (C_2-C_4), and still more preferably 2-3 carbon atoms (C_2-C_3). Examples of such alkynyl radicals include ethynyl, propynyl (propargyl), butynyl and the like.

"Alkoxy", alone or in combination, means a radical of the type "R-O-" wherein "R" is an alkyl radical as defined above and "O" is an oxygen atom. Examples of such alkoxy radicals include methoxy, ethoxy, n-propoxy, isopropoxy, n-butoxy, iso-butoxy, sec-butoxy, tert-butoxy and the like.

"Alkoxycarbonyl", alone or in combination, means a radical of the type "R-O-C(O)-" wherein "R-O-" is an alkoxy radical as defined above and "C(O)" is a carbonyl radical.

"Alkoxycarbonylamino", alone or in combination, means a radical of the type "R-O-C(O)-NH-" wherein "R-O-C(O)" is an alkoxycarbonyl radical as defined above, wherein the amino radical may optionally be substituted, such as with alkyl, aryl, aralkyl, cycloalkyl, cycloalkylalkyl and the like.

"Alkylthio", alone or in combination, means a radical of the type "R-S-" wherein "R" is an alkyl radical as defined above and "S" is a sulfur atom. Examples of such alkylthio radicals include methylthio, ethylthio, n-propylthio, isopropylthio, n-butylthio, iso-butylthio, sec-butylthio, tert-butylthio and the like.

"Alkylsulfinyl", alone or in combination, means a radical of the type "R-S(O)-" wherein "R" is an alkyl radical as defined above and "S(O)" is a mono-oxygenated sulfur atom. Examples of such alkylsulfinyl radicals include methylsulfinyl, ethylsulfinyl, n-propylsulfinyl, isopropylsulfinyl, n-butylsulfinyl, iso-butylsulfinyl, sec-butylsulfinyl, tert-butylsulfinyl and the like.

"Alkylsulfonyl", alone or in combination, means a radical of the type "R-$S(O)_2$-" wherein "R" is an alkyl radical as defined above and "$S(O)_2$" is a di-oxygenated sulfur atom. Examples of such alkylsulfonyl radicals include methylsulfonyl, ethylsulfonyl, n-propylsulfonyl, isopropylsulfonyl, n-butylsulfonyl, iso-butylsulfonyl, sec-butylsulfonyl, tert-butylsulfonyl and the like.

"Alkylsulfonylamino", alone or in combination, means a radical of the type "R-$S(O)_2$-NH-" wherein "R-$S(O)_2$-" is an alkylsulfonyl radical as defined above, wherein the amino radical may optionally be substituted, such as with alkyl, aryl, aralkyl, cycloalkyl, cycloalkylalkyl and the like.

"Aryl", alone or in combination, means a phenyl, biphenyl or naphthyl radical which is optionally substituted with one or more substituents selected from alkyl, alkoxy, halogen, hydroxy, amino, azido, nitro, cyano, haloalkyl, carboxy, alkoxycarbonyl, cycloalkyl, heterocyclo, alkanoylamino, amido, amidino, alkoxycarbonylamino, N-alkylamidino, alkylamino, dialkylamino, N-alkylamido, N,N-dialkylamido, aralkoxycarbonylamino, alkylthio, alkylsulfinyl, alkylsulfonyl and the like. Examples of aryl radicals are phenyl, p-tolyl, 4-methoxyphenyl, 4-(tert-butoxy)phenyl, 3-methyl-4-methoxyphenyl, 4-CF_3-phenyl, 4-fluorophenyl, 4-chlorophenyl, 3-nitrophenyl, 3-aminophenyl, 3-acetamidophenyl, 4-acetamidophenyl, 2-methyl-3-acetamidophenyl, 2-methyl-3-aminophenyl, 3-methyl-4-aminophenyl, 2-amino-3-methylphenyl, 2,4-dimethyl-3-aminophenyl, 4-hydroxyphenyl, 3-methyl-4-hydroxyphenyl, 4-(4-methoxyphenyl)phenyl, 1-naphthyl, 2-naphthyl, 3-amino-1-naphthyl, 2-methyl-3-amino-1-naphthyl, 6-amino-2-naphthyl, 4,6-dimethoxy-2-naphthyl, piperazinylphenyl and the like.

"Aryl-alkyl", alone or in combination, means an alkyl radical as defined above in which at least one hydrogen atom, preferably 1-2, is replaced by an aryl radical as defined above, such as benzyl, 1-, 2-phenylethyl, dibenzylmethyl, hydroxyphenylmethyl, methylphenylmethyl, diphenylmethyl, dichlorophenylmethyl, 2-naphthylmethyl, 4-methoxyphenylmethyl and the like.

"Aryl-alkoxy", alone or in combination, means an alkoxy radical as defined above in which at least one hydrogen atom, preferably 1-2, is replaced by an aryl radical as defined above, such as benzyloxy, 1-, 2-phenylethoxy, dibenzylmethoxy, hydroxyphenylmethoxy,

methylphenylmethoxy, dichlorophenylmethoxy, 4-methoxyphenylmethoxy and the like.

"Aryloxy", alone or in combination, means a radical of the type "R-O-" wherein "R" is an aryl radical as defined above.

"Aroyl", alone or in combination, means a radical of the type "R-C(O)-" wherein "R" is an aryl radical as defined above and "-C(O)-" is a carbonyl.

"Alkanoyl", alone or in combination, means a radical of the type "R-C(O)-" wherein "R" is an alkyl radical as defined above and "-C(O)-" is a carbonyl radical. Examples of such alkanoyl radicals include acetyl, trifluoroacetyl, hydroxyacetyl, propionyl, butyryl, valeryl, 4-methylvaleryl, and the like.

"Alkanoylamino", alone or in combination, means a radical of the type "R-C(O)-NH-" wherein "R-C(O)-" is an alkanoyl radical as defined above, wherein the amino radical may optionally be substituted, such as with alkyl, aryl, aralkyl, cycloalkyl, cycloalkylalkyl and the like.

"Aminocarbonylamino", alone or in combination, means an amino substituted carbonyl substituted on a second amino (ureido) radical, wherein each amino radical may optionally be mono- or di-substituted, such as with alkyl, aryl, aralkyl, cycloalkyl, cycloalkylalkyl, alkanoyl, alkoxycarbonyl, aralkoxycarbonyl and the like.

"Benzo", alone or in combination, means the divalent radical C_6H_4= derived from benzene.

"Bicyclic" as used herein is intended to include both fused ring systems, such as naphthyl and ß-carbolinyl,

and substituted ring systems, such as biphenyl, phenylpyridyl, naphthyl and diphenylpiperazinyl.

"Cycloalkyl", alone or in combination, means a saturated or partially saturated, preferably one double bond, monocyclic, bicyclic or tricyclic alkyl radical, preferably monocyclic, containing preferably 3-10 carbon atoms (C_3-C_{10}), more preferably 3-8 carbon atoms (C_3-C_8), even more preferably 3-6 carbon atoms (C_3-C_6), which is optionally be benzo fused and which is optionally substituted as defined herein with respect to the definition of aryl. Examples of such cycloalkyl radicals include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, dihydroxycyclohexyl, cycloheptyl, octahydronaphthyl, tetrahydronaphthyl, dimethoxytetrahydronaphthyl, 2,3-dihydro-1H-indenyl and the like.

"Cycloalkylene" is a cycloalkyl gem divalent radical, wherein cycloalkyl is as defined above. Preferably, cycloalkylene is monocyclic, containing preferably 3-10 carbon atoms (C_3-C_{10}), more preferably 3-8 carbon atoms (C_3-C_8), even more preferably 3-6 carbon atoms (C_3-C_6).

"Cycloalkylalkyl", alone or in combination, means an alkyl radical as defined above which is substituted by a cycloalkyl radical as defined above. Examples of such cycloalkylalkyl radicals include cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl, cyclohexylmethyl, 1-cyclopentylethyl, 1-cyclohexylethyl, 2-cyclopentylethyl, 2-cyclohexylethyl, hydroxycyclopentylpropyl, tetrahydronaphthylpropyl, cyclohexylbutyl and the like.

"Heteroatoms" means nitrogen, oxygen and sulfur heteroatoms.

"Heterocyclyl", alone or in combination, means a saturated or partially unsaturated, preferably one double bond, monocyclic or bicyclic, preferably monocyclic, heterocycle radical containing at least one, preferably 1 to 4, more preferably 1 to 3, even more preferably 1-2, nitrogen, oxygen or sulfur atom ring member and having preferably 3-8 ring members in each ring, more preferably 5-8 ring members in each ring and even more preferably 5-6 ring members in each ring. "Heterocyclyl" is intended to include sulfone and sulfoxide derivatives of sulfur ring members and N-oxides of tertiary nitrogen ring members, and carbocyclic fused, preferably 3-6 ring carbon atoms and more preferably 5-6 ring carbon atoms, and benzo fused ring systems. "Heterocyclyl" radicals may optionally be substituted on at least one, preferably 1-4, more preferably 1-3, even more preferably 1-2, carbon atoms by halogen, alkyl, alkoxy, hydroxy, oxo, thioxo, aryl, aralkyl, heteroaryl, heteroaralkyl, amidino, N-alkylamidino, alkoxycarbonylamino, alkylsulfonylamino and the like, and/or on a secondary nitrogen atom by hydroxy, alkyl, aralkoxycarbonyl, alkanoyl, alkoxycarbonyl, heteroaralkyl, aryl or aralkyl radicals. More preferably, "heterocyclyl", alone or in combination, is a radical of a monocyclic or bicyclic saturated heterocyclic ring system having 5-8 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally partially unsaturated or benzo-fused and optionally substituted by 1-2 oxo or thioxo radicals. Examples of such heterocyclyl radicals include pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiamorpholinyl, 4-benzyl-piperazin-1-yl, pyrimidinyl, tetrahydrofuryl, pyrazolidonyl, pyrazolinyl, pyridazinonyl, pyrrolidonyl, tetrahydrothienyl and its sulfoxide and sulfone derivatives, 2,3-dihydroindolyl, tetrahydroquinolinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydro-1-

oxo-isoquinolinyl, 2,3-dihydrobenzofuryl, benzopyranyl, methylenedioxyphenyl, ethylenedioxyphenyl and the like.

"Heterocyclylene" is a heterocyclyl gem divalent radical on a ring carbon atom, wherein heterocyclyl is as defined above. Preferably, heterocyclylene is a monocyclic saturated heterocyclic ring system having 5-6 ring members, wherein 1-3, more preferably 1-2, most preferably 1, ring members are oxygen, sulfur or nitrogen heteroatoms.

"Heterocyclylalkyl", alone or in combination, means an alkyl radical as defined above in which at least one hydrogen atom, preferably 1-2, is replaced by a heterocyclyl radical as defined above, such as pyrrolidinylmethyl, tetrahydrothienylmethyl, piperidinylethyl and the like.

"Heteroaryl", alone or in combination, means a monocyclic or bicyclic, preferably monocyclic, aromatic heterocycle radical, having at least one, preferably 1 to 4, more preferably 1 to 3, even more preferably 1-2, nitrogen, oxygen or sulfur atom ring members and having preferably 5-6 ring members in each ring, which is optionally benzo fused or saturated carbocyclic fused, preferably 3-4 carbon atoms (C_3-C_4) to form 5-6 ring membered rings and which is optionally substituted as defined above with respect to the definitions of aryl and heterocyclyl. More preferably, "heteroaryl", alone or in combination, is a radical of a monocyclic or bicyclic aromatic heterocyclic ring system having 5-6 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally benzo-fused or saturated C_3-C_4-carbocyclic-fused. Examples of such heteroaryl groups include imidazolyl, 1-benzyloxycarbonylimidazol-4-yl, pyrrolyl, pyrazolyl, pyridyl, 2-(1-piperidinyl)pyridyl, 2-(4-

benzyl piperazin-1-yl)-1-pyridinyl, pyrazinyl, triazolyl, furyl, thienyl, oxazolyl, thiazolyl, indolyl, quinolinyl, 1-oxido-2-quinolinyl, isoquinolinyl, 5,6,7,8-tetrahydroquinolyl, 5,6,7,8-tetrahydroiso-quinolinyl, quinoxalinyl, benzothiazolyl, ß-carbolinyl, benzofuryl, benzimidazolyl, benzoxazolyl and the like.

"Heteroaroyl", alone or in combination, means a radical of the type "R-C(O)-" wherein "R" is an heteroaryl radical as defined above and "-C(O)-" is a carbonyl.

"Heteroaryl-alkyl", alone or in combination, means an alkyl radical as defined above in which at least one hydrogen atom, preferably 1-2, is replaced by a heteroaryl radical as defined above, such as 3-furyl-propyl, 2-pyrrolylpropyl, chloroquinolinylmethyl, 2-thienylethyl, pyridylmethyl, 1-imidazolylethyl and the like.

"Halogen" and "halo", alone or in combination, means fluoro, chloro, bromo or iodo radicals.

"Haloalkyl", alone or in combination, means an alkyl radical as defined above in which at least one hydrogen atom, preferably 1-3, is replaced by a halogen radical, more preferably fluoro or chloro radicals. Examples of such haloalkyl radicals include 1,1,1-trifluoroethyl, chloromethyl, 1-bromoethyl, fluoromethyl, difluoro-methyl, trifluoromethyl, bis(trifluoromethyl)methyl and the like.

"Haloalkoxy", alone or in combination, means an alkoxy radical as defined above in which at least one hydrogen atom, preferably 1-3, is replaced by a halogen radical, more preferably fluoro or chloro radicals. Examples of such haloalkoxy radicals include 2,2,2-trifluoroethoxy, chloromethoxy, 2-bromoethoxy, fluoromethoxy, difluoro-

methoxy, trifluoromethoxy, bis(trifluoromethyl)methoxy and the like.

"Sulfinyl", alone or in combination, means a diradical of the type "-S(O)-" wherein "S(O)" is a mono-oxygenated sulfur atom. "Sulfonyl", alone or in combination, means a diradical of the type "-$S(O)_2$-" wherein "$S(O)_2$" is a di-oxygenated sulfur atom.

"Leaving group" generally refers to groups readily displaceable by a nucleophile, such as an amine, a thiol or an alcohol nucleophile. Such leaving groups are well known in the art. Examples of such leaving groups include, but are not limited to, N-hydroxysuccinimide, N-hydroxybenzotriazole, halides, triflates, tosylates and the like. Preferred leaving groups are indicated herein where appropriate.

"Protecting group" generally refers to groups well known in the art which are used to prevent selected reactive groups, such as carboxy, amino, hydroxy, mercapto and the like, from undergoing undesired reactions, such as nucleophilic, electrophilic, oxidation, reduction and the like. Preferred protecting groups are indicated herein where appropriate. Examples of amino protecting groups include, but are not limited to, aralkyl, substituted aralkyl, cycloalkenylalkyl and substituted cycloalkenyl alkyl, allyl, substituted allyl, acyl, alkoxycarbonyl, aralkoxycarbonyl, silyl and the like. Examples of aralkyl include, but are not limited to, benzyl, ortho-methylbenzyl, trityl and benzhydryl, which can be optionally substituted with halogen, alkyl, alkoxy, hydroxy, nitro, acylamino, acyl and the like, and salts, such as phosphonium and ammonium salts. Examples of aryl groups include phenyl, naphthyl, indanyl, anthracenyl, 9-(9-phenylfluorenyl), phenanthrenyl, durenyl and the like. Examples of

cycloalkenylalkyl or substituted cycloalkylenylalkyl radicals, preferably have 6-10 carbon atoms, include, but are not limited to, cyclohexenyl methyl and the like. Suitable acyl, alkoxycarbonyl and aralkoxycarbonyl groups include benzyloxycarbonyl, t-butoxycarbonyl, iso-butoxycarbonyl, benzoyl, substituted benzoyl, butyryl, acetyl, tri-fluoroacetyl, tri-chloro acetyl, phthaloyl and the like. A mixture of protecting groups can be used to protect the same amino group, such as a primary amino group can be protected by both an aralkyl group and an aralkoxycarbonyl group. Amino protecting groups can also form a heterocyclic ring with the nitrogen to which they are attached, for example, 1,2-bis(methylene)benzene, phthalimidyl, succinimidyl, maleimidyl and the like and where these heterocyclic groups can further include adjoining aryl and cycloalkyl rings. In addition, the heterocyclic groups can be mono-, di- or tri-substituted, such as nitrophthalimidyl. Amino groups may also be protected against undesired reactions, such as oxidation, through the formation of an addition salt, such as hydrochloride, toluenesulfonic acid, trifluoroacetic acid and the like. Many of the amino protecting groups are also suitable for protecting carboxy, hydroxy and mercapto groups. For example, aralkyl groups. Alkyl groups are also sutiable groups for protecting hydroxy and mercapto groups, such as tert-butyl.

Silyl protecting groups are silicon atoms optionally substituted by one or more alkyl, aryl and aralkyl groups. Suitable silyl protecting groups include, but are not limited to, trimethylsilyl, triethylsilyl, tri-isopropylsilyl, tert-butyldimethylsilyl, dimethylphenylsilyl, 1,2-bis(dimethylsilyl)benzene, 1,2-bis(dimethylsilyl)ethane and diphenylmethylsilyl. Silylation of an amino groups provide mono- or di-silylamino groups. Silylation of aminoalcohol compounds can lead to a N,N,O-tri-silyl

derivative. Removal of the silyl function from a silyl ether function is readily accomplished by treatment with, for example, a metal hydroxide or ammonium flouride reagent, either as a discrete reaction step or in situ during a reaction with the alcohol group. Suitable silylating agents are, for example, trimethylsilyl chloride, tert-buty-dimethylsilyl chloride, phenyldimethylsilyl chloride, diphenylmethyl silyl chloride or their combination products with imidazole or DMF. Methods for silylation of amines and removal of silyl protecting groups are well known to those skilled in the art. Methods of preparation of these amine derivatives from corresponding amino acids, amino acid amides or amino acid esters are also well known to those skilled in the art of organic chemistry including amino acid/amino acid ester or aminoalcohol chemistry.

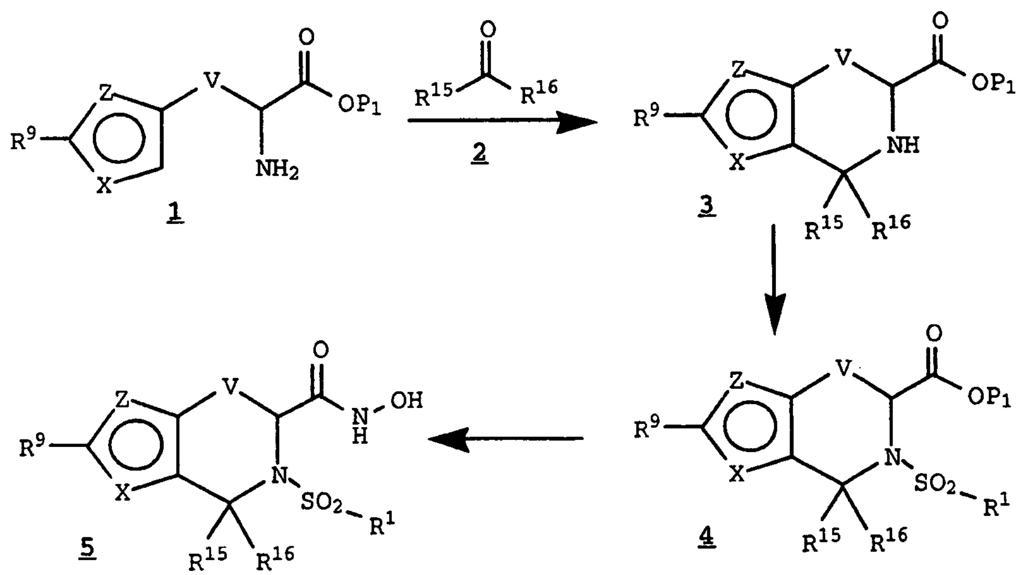
Protecting groups are removed under conditions which will not affect the remaining portion of the molecule. These methods are well known in the art and include acid hydrolysis, hydrogenolysis and the like. A preferred method involves removal of a protecting group, such as removal of a benzyloxycarbonyl group by hydrogenolysis utilizing palladium on carbon in a suitable solvent system such as an alcohol, acetic acid, and the like or mixtures thereof. A t-butoxycarbonyl protecting group can be removed utilizing an inorganic or organic acid, such as HCl or trifluoroacetic acid, in a suitable solvent system, such as dioxane or methylene chloride. The resulting amino salt can readily be neutralized to yield the free amine. Carboxy protecting group, such as methyl, ethyl, benzyl, tert-butyl, 4-methoxyphenylmethyl and the like, can be removed under hydroylsis and hydrogenolysis conditions well known to those skilled in the art.

Procedures for preparing the compounds of this invention are set forth below. It should be noted that the general procedures are shown as it relates to preparation of compounds having unspecified stereochemistry. However, such procedures are generally applicable to those compounds of a specific stereochemistry, e.g., where the stereochemistry about a group is (S) or (R). In addition, the compounds having one stereochemistry (e.g., (R)) can often be utilized to produce those having opposite stereochemistry (i.e., (S)) using well-known methods, for example, by inversion.

Preparation of Compounds of Formula I

The compounds of the present invention represented by Formula I above can be prepared utilizing the following general procedures as schematically shown in Schemes I and II.

SCHEME I

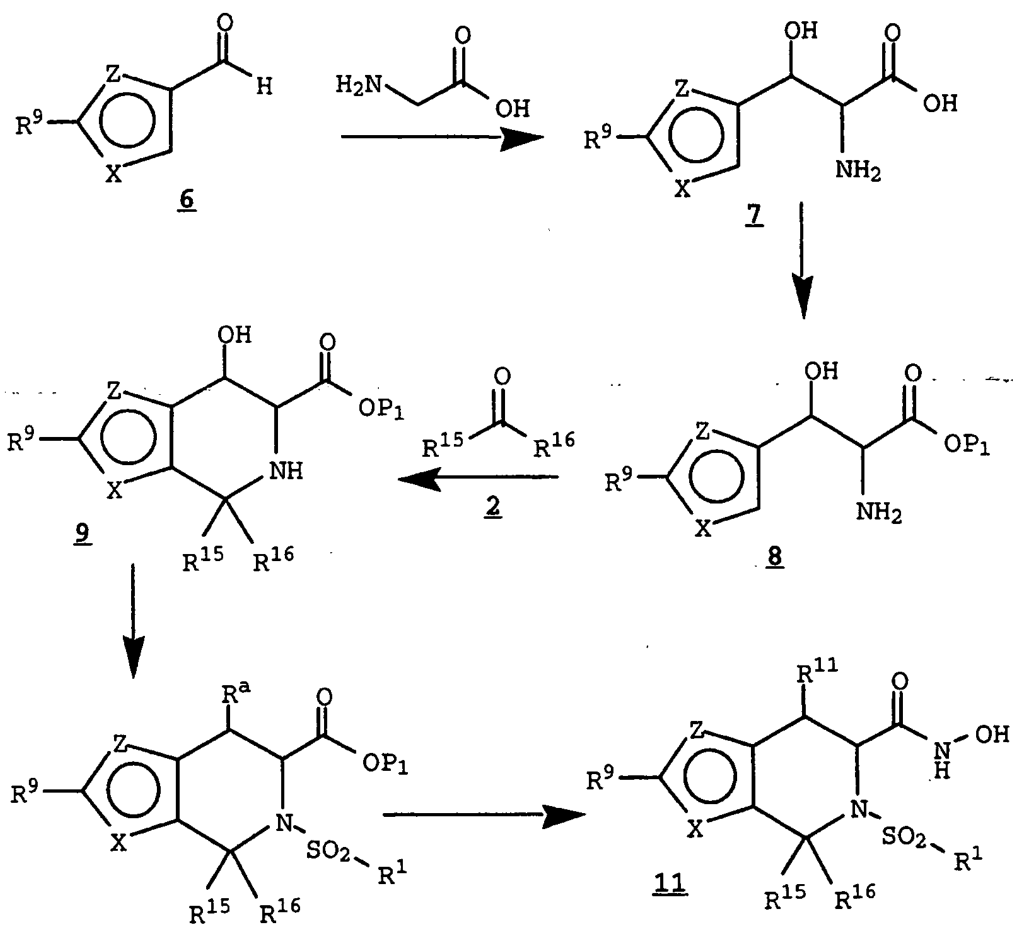


Compounds of the present invention may be synthesised using the routes outlined in Schemes I

through IV. An appropriately substituted protected (for example, P_1 is a methyl, ethyl, benzyl and the like) or unprotected (P_1 is H) amino acid (1) upon treatment with appropriately functionalized aldehydes or ketones (2) under acidic conditions (for example see Sola, R. et al, J. Heterocycles, 19, 1982), can give the bicyclic intermediate (3). The acid functionality of the bicyclic intermediate (3) (when P_1 is H) is then be converted into an ester using standard procedures (for example HCl and methanol). The protected bicyclic intermediate (3) is then sulfonylated under Schotten-Baumann conditions to furnished the sulfonamide (4). Sulfonamide (4) (when R^9 is H) may be halogenated, such as iodinated, and then carbonylated (See for example Schoenberg, A., et al, J.Org.Chem., 39, 3318, (1974))) and subsequently derivatised, amidated (See for example Corey, E.J. and Hegedus, L.S., J.Am.Chem.Soc., 91, 1233 (1969)), arylated or alkylated (See for example Stille, J.K., Angew. Int. Ed. Engl., 25, 508 (1986)) to yield sulfonamide (4) where R^9 is other than H. Sulfonamide (4) can be readily converted into the corresponding hydroxamic acids (5) using procedures well known to those skilled in the art. Alternatively, R^{11} and/or R^{12} may be introduced into sulfonamide (4), where R^{11} and/or R^{12} are independently a leaving group (L′ and L″, respectively) utilizing suitably functionalized nucleophilic species (such as $R^{21}SH$ or $R^{33}NH_2$ followed by reaction with the electrophile $R^{31}N{=}C{=}O$, $R^{32}R^{31}N\text{-}C(O)\text{-}L$, $R^{31}\text{-}C(O)\text{-}L$, $R^{30}\text{-}SO_2\text{-}L$, $R^{32}R^{31}N\text{-}SO_2\text{-}L$, and the like) and/or a hydroxy, amino, substituted amino or thiol group utilizing suitably functionalized electrophilic species (such as $R^{31}N{=}C{=}O$, $R^{32}R^{31}N\text{-}C(O)\text{-}L$, $R^{20}\text{-}L$, $R^{22}\text{-}C(O)\text{-}L$ and the like), where L, L′ and L″ are each a leaving group, such as chloro, bromo, iodo, mesylate, tosylate and the like. When R^{11} or R^{12} is a hydroxy, amino, substituted amino or thiol group, the groups may require selective protection and de-protection, using reagents and methods well known

in the art, in order to avoid producing undesired reaction products.

SCHEME II

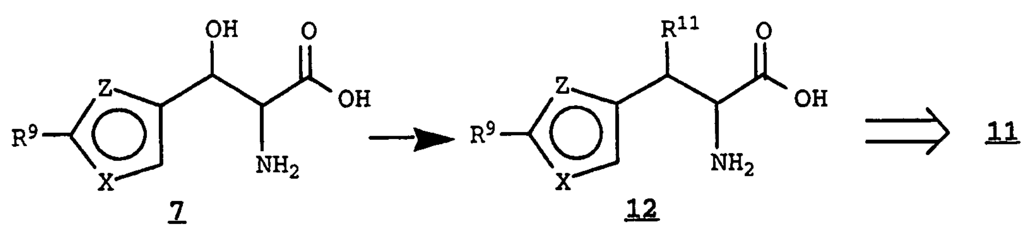


10a R^a = -OH
10b R^a = $-R^{11}$
10c R^a = -L

Alternatively, an appropriately substituted heterocyclic carboxaldehyde (6) (Scheme II) may be condensed, under basic conditions, with a glycine to give the hydroxy amino acid (7) (See for example Dullaghan, M.E. and Nord, F.F., J.Am.Chem.Soc., 73, 5455 (1951)). The hydroxy amino acid (7) is then protected (for example, esterified) to yield the protected amino acid (8). Cyclization of the protected amino acid (8) under acidic conditions with an appropriately

functionalized aldehyde or ketone (2) can furnish the bicyclic intermediate (9). Sulfonylation, using Schotten-Baumann conditions, of the bicyclic intermediate (9) can give the sulfonamide (10a). Sulfonamide (10a) can be readily converted into the corresponding hydroxamic acid (11), where R^{11} is -OH, using procedures well known to those skilled in the art. Alternatively, sulfonamide (10a) may be derivatized by treatment with a suitably functionalized electrophilic species, such as $R^{31}N{=}C{=}O$, $R^{32}R^{31}N\text{-}C(O)\text{-}L$, $R^{20}\text{-}L$, $R^{22}\text{-}C(O)\text{-}L$ and the like, where L is a leaving group, such as chloro, bromo, iodo, mesylate, tosylate and the like, to generate sulfonamide (10b). (See for example Duggan, M.E. and Imagrire J.S., Synthesis 131 (1989)). Sulfonamide (10b) can be readily converted into the corresponding hydroxamic acid (11) using procedures well known to those skilled in the art. Alternatively, the hydroxy group of sulfonamide (10a) may be converted into a leaving group (R^a = L) by treatment with a suitable agents well known to those skilled in the art, such as halogenating agents (for example PCl_5, PBr_3, and the like), mesyl chloride, tosyl chloride, and the like, where L is a leaving group, such as chloro, bromo, iodo, mesylate, tosylate and the like, to generate sulfonamide (10c). The leaving group (L) of sulfonamide (10c) can be displaced with a nucleophile, such as $R^{21}SH$ or $R^{33}NH_2$ followed by reaction with the electrophile $R^{31}N{=}C{=}O$, $R^{32}R^{31}N\text{-}C(O)\text{-}L$, $R^{31}\text{-}C(O)\text{-}L$, $R^{30}\text{-}SO_2\text{-}L$, $R^{32}R^{31}N\text{-}SO_2\text{-}L$, and the like, to prepare sulfonamide (10b).

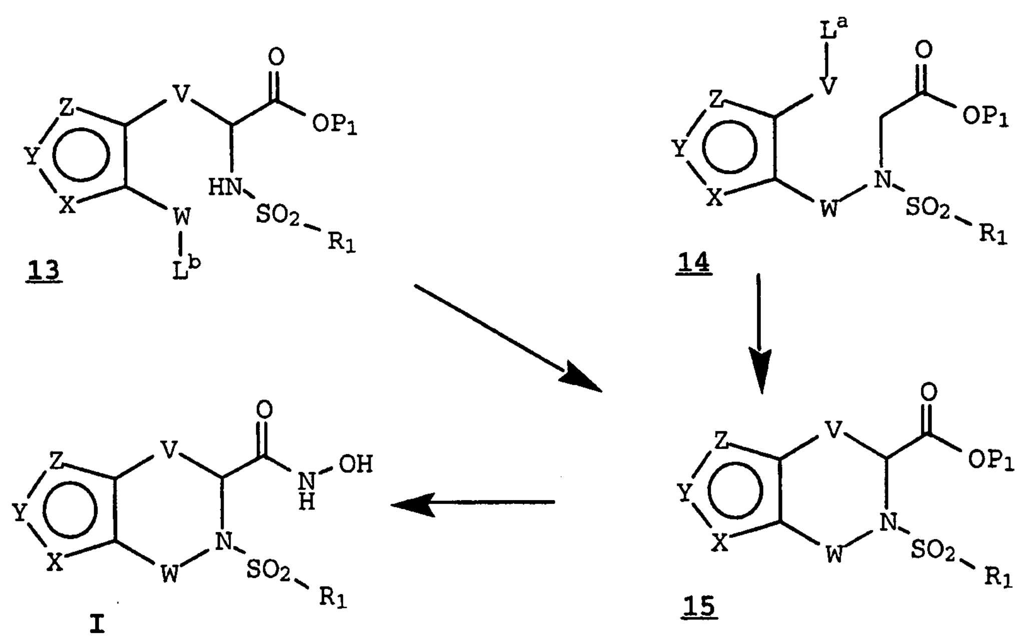
SCHEME III



Alternatively, hydroxy amino acid (7) may be converted with nucleophiles, electrophiles and the like as described above or under Mitsonobu conditions to yield the amino acid intermediate (12) (Scheme III). The amino acid intermediate (12) may subsequently be cyclised, sulfonylated and converted to hydroxamic acids using the aforementioned procedures to give hydroxamic acid (11).

Alternatively, sulfonamides (10a) or (10b) (when R^9 is H) may be halogenated, such as iodinated, and then carbonylated (See for example Schoenberg, A., et al, J.Org.Chem., 39, 3318, (1974))) and subsequently derivatised, amidated (See for example Corey, E.J. and Hegedus, L.S., J.Am.Chem.Soc., 91, 1233 (1969)), arylated or alkylated (See for example Stille, J.K., Angew. Int. Ed. Engl., 25, 508 (1986)) to yield sulfonamides (10a) or (10b) where R^9 is other than H.

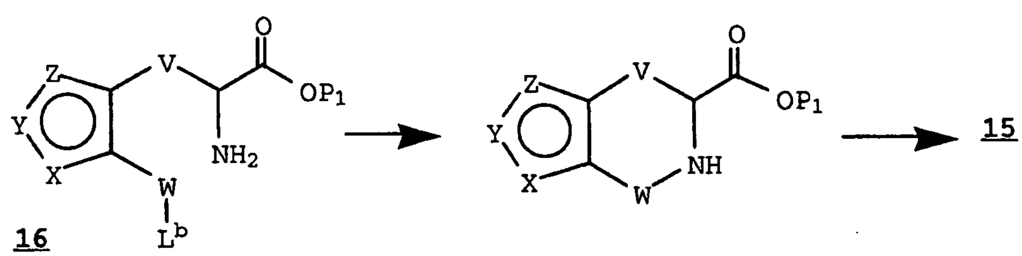
SCHEME IV



A second general synthesis useful for the preparation of the novel compounds of this invention is illustrated in Scheme IV whereby an appropriately

substituted heterocycle (13) or (14) is cyclized into bicyclic intermediate (15) in the presence of a base, such as KOH in THF, potassium carbonate in DMF, and the like, where L^a and L^b are each a leaving group, such as chloro, bromo, iodo, mesylate, tosylate and the like, or $-V-L^a$ is an appropriately substituted ketone or aldehyde group, or $-V-L^a$ or $-W-L^b$ is an appropriately substituted unsaturated aldehyde, ketone, ester, amide, nitrile or the like Michael reaction acceptor, or other cyclization method well known to those skilled in the art. Alternatively, the bicyclic intermediate (15) can be prepared in two steps from a protected amino acid (16) wherein the R^1-SO_2- group is introduced after cyclization with the amino group ($-NH_2$) (see Scheme V). When appropriate R^8, R^9, R^{10}, R^{11}, R^{12}, R^{15}, R^{16}, R^{17} and R^{18} may be introduced prior to or after the cyclization step provided the radicals do not interfer with, compete with or inhibit the cyclization reaction. One skilled in the art is well versed in such matters and knows when and how to introduce the various groups and utilize protecting groups to prevent such deleterious effects.

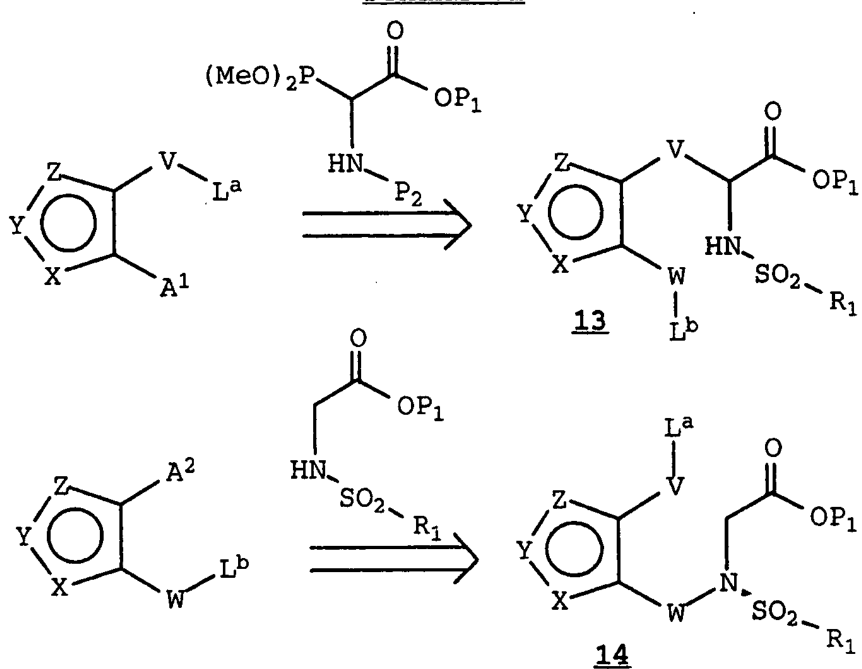
SCHEME V



The intermediates (13), (14) and (16) are readily prepared from commercially available starting materials, for example as shown in Scheme VI, wherein P^1 and P^2 are protecting groups, L^a and L^b are leaving groups, A^1 is a radical that can converted into $-W-L^b$ and A^2 is a radical that can be converted into $-V-L^a$.

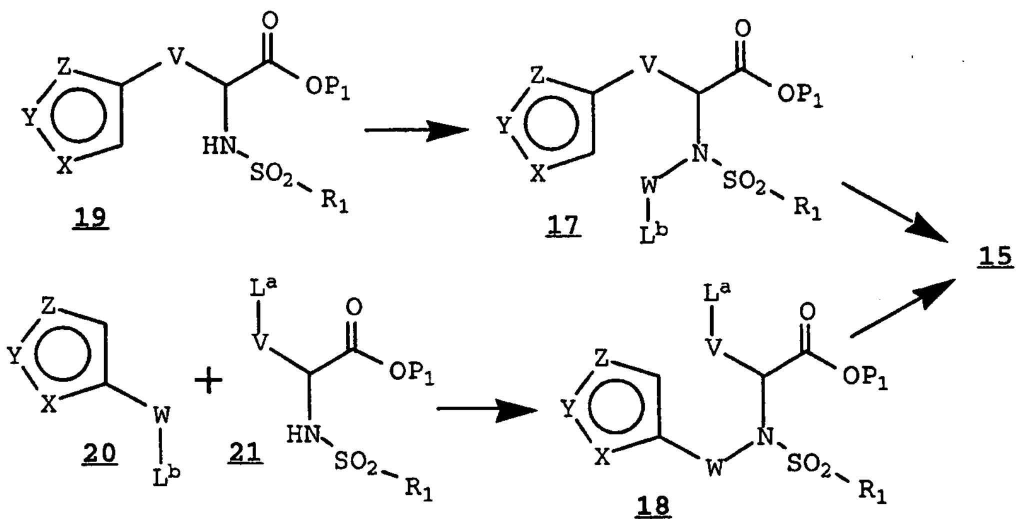
A third general synthesis useful for the preparation of the novel compounds of this invention is cyclization reactions, such as Friedel-Crafts and the like reactions, directly onto the heterocyclic ring as illustrated in Scheme VII, whereby an appropriately substituted heterocycle (17) or (18) is cyclized into bicyclic intermediate (15) by nucleophilic displacement of the leaving group L^a or L^b, such as in the presence of acid or a Friedel-Crafts reagent, such as tin chloride, aluminum chloride and the like, or other nucleophilic reaction conditions, such as formation of an anion on the ring, for example, metal halogen exchange and the like. (For an example of Friedel Crafts reaction, see Frehel, D, Badorc, A., Pereillo, J-M, Maffrand, J-P J Heterocycl Chem 1985, 22, 1011-1016) In such reactions, $-W-L^b$ and $-V-L^a$ are groups containing an electrophilic group, such as halogen (Cl, Br, I), ester, carboxylic acid, carboxylic acid halide, aldehyde, ketone, nitrile and the like.

SCHEME VI



Heterocycle (17) can be prepared from the sulfonamide (19) by reaction with L^b-W-L^c or A^1-L^c wherein A^1 is a radical that can be coverted into -W-L^b and wherein L^c is a leaving group similar to L^a and L^b. Sulfonamide (19) can be readily prepared from the corresponding protected or unprotected amino acid by reaction with the appropriate sulfonyl chloride (R^1-SO_2-Cl) or the like. The amino acid is either commercially available or is readily prepared from commercially available starting materials using methods well known to those skilled in the art.

SCHEME VII



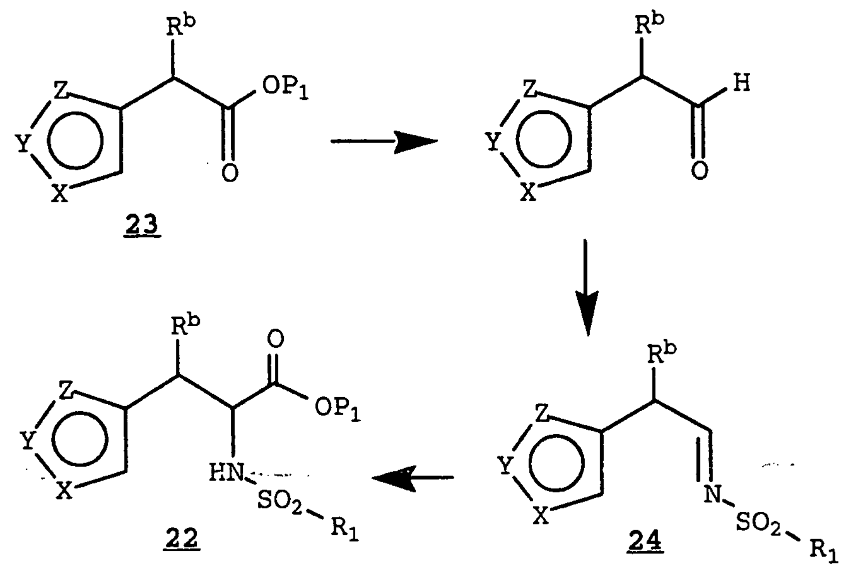
Heterocycle (18) can be prepared by coupling the electrophile (20) with the sulfonamide (21) in the presence of a base, such as potassium carbonate and the like. The radical A^2 may be used in place of -V-L^a in sulfonamide (21) to avoid reaction of -V-L^a with the sulfonamide group, in which event A^2 is converted into -V-L^a after reaction of the electrophile (20) with the sulfonamide (21). Electrophiles (20) are either commercially available or is readily prepared from commercially available starting materials using

methods well known to those skilled in the art. Sulfonamide (21) can be prepared from the corresponding protected or unprotected amino acid by reaction with the appropriate sulfonyl chloride (R^1-SO_2-Cl) or the like. The amino acid is either commercially available or is readily prepared from commercially available starting materials using methods well knoen to those skilled in the art.

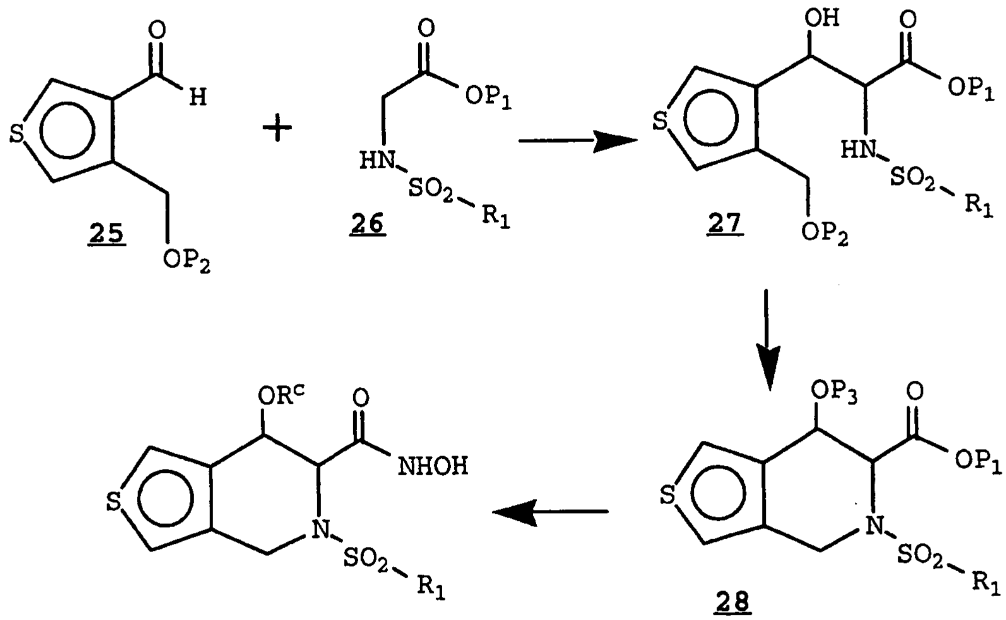
Alternatively, protected or unprotected sulfonamide intermediate (22), wherein R^b is R^{11} or a group which can be converted into R^{11} during the synthesis of the compounds of this invention, may be prepared from a substituted protected carboxylic acid intermediate (23) (Scheme VIII). The carboxylic acid intermediate (23) can be selectively reduced to an aldehyde using appropriate reducing agents, such as DIBAL-H and the like, which is converted into the sulfonamide imine (24) by reaction of the aldehyde with the the sulfonamide $R^1SO_2NH_2$ using reaction conditions well known in the art. The sulfonamide imine (24) can then be reacted with a carbon nucleophile which can be converted into a carboxylic acid or ester, such as cyanide anion followed by hydrolysis, 1,3-dithiane anion followed by deprotection and oxidation, and the like, to yield the protected or unprotected sulfonamide intermediate (22).

The substituted protected carboxylic acid intermediate (23) is commercially available or may be readily prepared from commercially available starting materials using methods well known to those skilled in the art. For instance, Perkin condensation between heterocyclic acetic acids and aldehydes to give an unsaturated acid followed by hydrogenation, Michael reaction, allylic rearrangement and the like, aldol condensation, alkylation and the like can be used to produce intermediate (23) from readily available

SCHEME VIII



SCHEME IX



29a R^c = -H

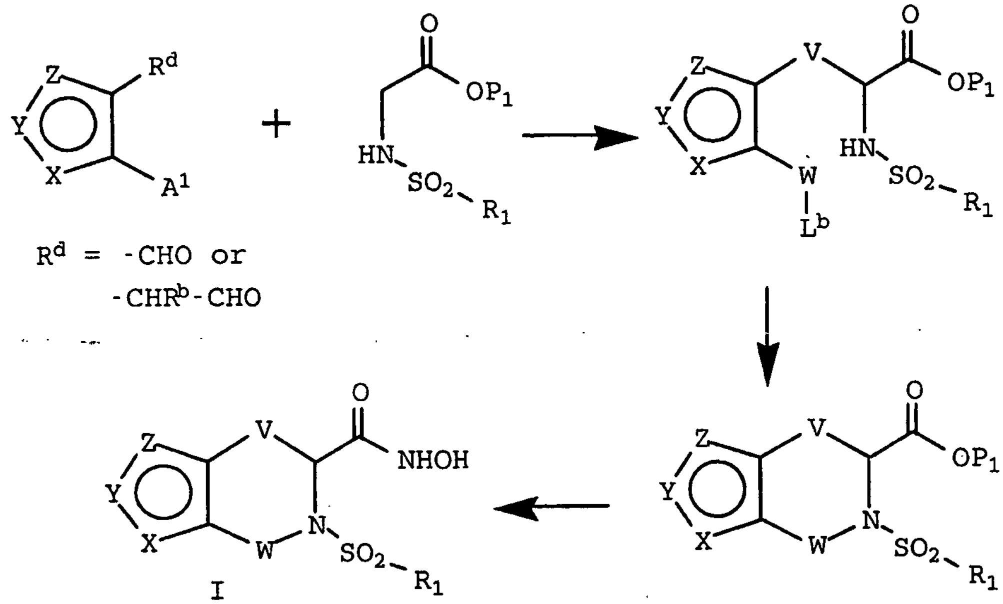
29b R^c = -C(O)$NR^{32}R^{31}$

29c R^c = -R^{20}

starting materials. Alternatively, unsubstituted (i.e., R^b = H) protected or unprotected carboxylic acid

intermediate (23) may be alkylated with electrophiles such as R^b-L, wherein L is a leaving group such as halogen, mesylate, tosylate, etc.

SCHEME X



For example, as shown in Scheme IX, an appropriately 3,4-substituted thiophene carboxaldehye (25), wherein P_2 is a hydroxy protecting group, may be condensed, under basic conditions (for example in the presence of LDA in THF) with a protected N-sulphonylated glycine (26), wherein P_1 is a carboxylic acid protecting group such as an ester and the like, to give beta-hydroxy amino acid (27) (see for example Dikshit, D.K., et al. Tet. Lett. 1988, 29(25), 3109-3110). The beta-hydroxy amino acid (27) may then be protected with a hydroxy protecting group P_3 such as by acylation of the beta-hydroxy group and separated into threo and erythro diastereomers. P_2 may then be removed and Mitsonobu cyclization conditions can give intermediate (28). P_1 may then be removed, a hydroxamic acid formed and P_3 removed to give (29a) utilizing methodology familiar to one skilled in the art. Alternatively, (28) may be deprotected to the

beta-hydroxy acid and converted to beta-carbamoyl hydroxamate (29b) or other substituted oxy group (i.e., $-OR^{20}$) compound (29c) again utilizing methodology familiar to one skilled in the art. This general scheme is also applicable for other substituted heterocyclic carboxaldehydes as shown in Scheme X to form six, seven and eight membered heterocyclic fused compounds (I) of this invention.

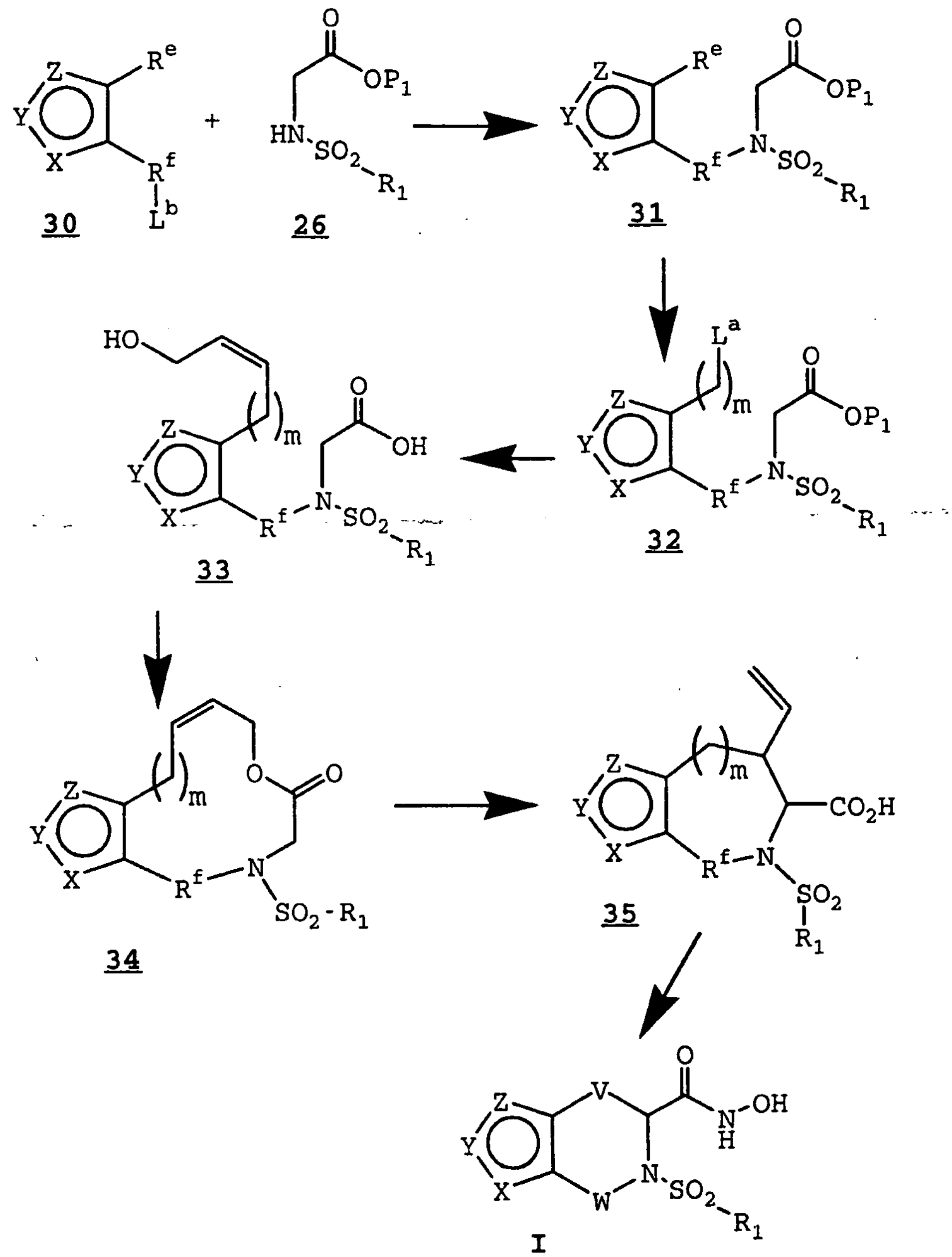
Scheme XI illustrates an alternative general synthesis (Claisen ring contraction) useful for the preparation of the novel compounds of this invention as illustrated in Scheme IV whereby an appropriately substituted heterocycle (14) is cyclized into bicyclic intermediate (15). As shown in Scheme XI, heterocycle (31) can be prepared by coupling electrophile (30), wherein R^e is $-(CH_2)_m-L^a$ (m = 0-1) or a group which can be converted into $-(CH_2)_m-L^a$ and wherein R^f is W or a group which can be converted into W during the synthesis of the compounds of this invention, with the protected N-sulphonylated glycine (26), wherein P_1 is a carboxylic acid protecting group such as an ester and the like, (for example, a Mitsunobu coupling, Syn. 1981:1-28). When R^e is a leaving group, such as bromine atom, R^e can be converted into $-(CH_2)_m-L^a$ by a homologation sequence (for example, for m = 1 and L^a = Br, Palladium catalyzed Stille coupling of tributylvinyltin with the heterocycle (31) (R^e = Br), followed by oxidative cleavage (OsO_4, $NaIO_4$) of the resulting vinyl group to form an aldehyde group (R^e = -CHO), reduction with $NaBH_4$ to an alcohol group (R^e = $-CH_2OH$), and finally bromination of the alcohol (NBS and PPh_3) to form the desired heterocycle (32) (m = 1, L^a = Br)).

The Z-allylic alcohol (33) can be prepared by coupling (Z)-$Bu_3SnCH=CHCH_2OTBS$, which has been synthesized and utilized in both its protected and unprotected forms (Corey et al., Tet. Lett. 25:2419-2422 (1984); Jung et al., Tet. Lett. 23:3851-3854 (1982); and

Stille et al., J. Am. Chem. Soc. 109:813-817 (1987)), with heterocycle (32). The coupling can be performed utilizing $PdCl_2(PPh_3)_2$ catalyzed Stille reaction (Stille, Chem. Int. Ed. Engl. 25:508-524 (1986); and Stille et al., J. Am. Chem. Soc. 101:4992-4998 (1979)). Alternatively, (Z)-$Bu_3SnCH=CHCH_2OTBDMS$ (prepared from commercially available ethyl cis-3-iodoarylate by reduction with about two equivalents of DIBAL-H (Beruben et al., J. Org. chem. 60:2488-2501 (1995)) by slow addition at about -78°C to minimize double bond isomerization during the reaction followed by gradual warming to ambient temperature, the resulting iodo-alcohol is protected as its TBDMS ether and then subjected to halogen-metal exchange (butyl lithium and tributyltin chloride, Pearson et al., J. Org. Chem. 59:5662-5671 (1994)) to give the desired (Z)-$Bu_3SnCH=CHCH_2OTBDMS$) is utilized in the coupling reaction. The Z-allylic alcohol (33) then results following deprotection of the carboxylic acid (such as with KOH in THF) and the TMS group (such as with acid) or the TBDMS group (such as with TBAF in THF).

The lactone (34) is then prepared from the Z-allylic alcohol (33). Many methods that are available to form medium to large lactones (Meng et al., "Topics in Current Chemistry, Ring Closure Methods in the Synthesis of Macrocyclic Natural Products," Springer-Verlag (Pub.), Vol. 161 (1991); and Nicolaou, Tetrahedron 33:683-710 (1977)). For example, the lactone (34) can be prepared from the Z-allylic alcohol (33) utilizing Mukaiyama's reagent (Mukaiyama et al., Chem. Lett. 1976:49-50; and Mukaiyama, Chem. Int. Ed. Engl. 18:707-721 (1979)) under high dilution conditions (Funk et al., J. Org. Chem. 49:4320-4322 (1984); Cooper et al., J. Chem. Soc., Chem. Commun., 1987:1220; and Cooper et al., Tet. Lett. 28:3031 (1987)).

SCHEME XI



Claisen ring contraction of the lactone (34) can be effected by treatment of the lactone with various combinations of reagents including TBDMSCl/LDA, TBDMSOTf/LHMDS and TBDMSOTf/KHMDS, such as in THF at about -78°C (Ireland et al., J. Am. Chem. Soc. 98:2868-2877 (1976)) followed by heating the reaction, for example to reflux, to give the Claisen product as a

protected carboxylic acid which can be deprotected, such as with , to yield the heterocycle carboxylic acid (35). Any silyl ester of the heterocycle carboxylic acid (35) produced in the reaction can be removed by treatment with aqueous K_2CO_3 in THF-MeOH to give the free the heterocycle carboxylic acid (35).

The relative stereochemistry between the vinyl and carboxylic acid groups of the heterocycle carboxylic acid (35) may be cis (Abelman et al., J. Am. Chem. Soc. 104:4030-4032 (1982); Funk et al., Tetrahedron 42:2831-2845 (1986); and Corey et al., J. Am. Chem. Soc. 118:1229-1230 (1996)). The carboxylic acid group of the heterocycle carboxylic acid (35) or the corresponding ester can be epimerized, for example by treatment with base, and the resulting cis and trans diasteriomers can be separated and the R and S enantiomers can be separated using methods well known to those skilled in the art. The 2-trimethylsilylethyl protecting group can be removed from the carboxylic acid group without substantial epimerization from the cis stereochemistry with fluoride in the presence of DMAP. The hydroxamic acids (I) of this invention can then be prepared from the heterocycle carboxylic acid (35) using PyBroP, $NH_2OH{\bullet}HCl$ and Hunigs base in CH_2Cl_2.

The alkene group of the heterocycle carboxylic acid (35) can be functionalize using methods well known in the art to produce a variety of groups. A recent methodology described by Suzuki et al. (Chem. Rev. 95:2457-2483 (1995)), which involves palladium catalyzed coupling of alkylborane derivatives with alkenyl or aryl halides or triflates. For example, coupling of the hydroboration product of an ester of heterocycle carboxylic acid (35) with iodobenzene can yield heterocycles substituted with a phenethyl group. This functionalization can be carried out in one pot by hydroboration with 9-BBN in THF, to give a terminally

substituted alkyl borane that is then treated with iodobenzene, K_2CO_3 and catalytic $PdCl_2$(dppf).

It is apparent from the above description that no single general synthesis can be used in the preparation of all of the novel compounds of this invention, because some of the radicals, well known to those skilled in the art, will or may have the potential of interfering with, competing with or inhibiting the some of the reactions involved in the pathway. However, one skilled in the art is fully aware of appropriate point in the synthetic pathway when a radical may be introduced and when protecting groups can be used.

Sulfonyl halides can be prepared by the reaction of a suitable alkyl, aryl, heteroaryl, heterocyclyl and the like Grignard or lithium reagents with sulfuryl chloride, or sulfur dioxide followed by oxidation with a halogen, preferably chlorine. Alkyl, heteroaryl, heterocyclyl, aryl and the like Grignard or lithium reagents can be prepared from their corresponding halide (such as chloro or bromo) compounds which are commercially available or readily prepared from commercially available starting materials using known methods in the art. Alternatively, mercaptans may be oxidized to sulfonyl chlorides using chlorine in the presence of water under carefully controlled conditions. Additionally, sulfonic acids may be converted into sulfonyl halides using reagents such as PCl_5, $SOCl_2$, ClC(O)C(O)Cl and the like, and also to anhydrides using suitable dehydrating reagents. The sulfonic acids are either commercially available or may be prepared using procedures well known in the art from commercially available starting materials. In place of the sulfonyl halides, sulfinyl halides or sulfenyl halides can be utilized to prepare compounds wherein the sulfonyl moiety is replaced by an sulfinyl or thio moiety, respectively. Arylsulfonic acids, benzo fused heterocyclyl sulfonic acids or heteroaryl sulfonic acids

can be prepared by sulfonation of the aromatic ring by well known methods in the art, such as by reaction with sulfuric acid, SO_3, SO_3 complexes, such as DMF(SO_3), pyridine(SO_3), N,N-dimethylacetamide(SO_3), and the like. Preferably, such sulfonyl halides are prepared from such aromatic compounds by reaction with DMF(SO_3) and $SOCl_2$ or ClC(O)C(O)Cl. The reactions may be performed stepwise or in a single pot.

Alkyl sulfonic acids, aryl sulfonic acids, heterocyclyl sulfonic acids, heteroaryl sulfonic acids, alkylmercaptans, arylmercaptans, heterocyclylmercaptans, heteroarylmercaptans, alkylhalides, arylhalides, heterocyclylhalides, heteroarylhalides, and the like are commercially available or can be readily prepared from starting materials commercially available using standard methods well known in the art.

Thioether derivatives can be converted into the corresponding sulfone or sulfoxide by oxidizing the thioether derivative with a suitable oxidation agent in a suitable solvent. Suitable oxidation agents include, for example, hydrogen peroxide, sodium meta-perborate, oxone (potassium peroxy monosulfate), meta-chloroperoxybenzoic acid, periodic acid and the like, including mixtures thereof. Suitable solvents include acetic acid (for sodium meta-perborate) and, for other peracids, ethers such as THF and dioxane, and acetonitrile, DMF and the like, including mixtures thereof.

The chemical reactions described above are generally disclosed in terms of their broadest application to the preparation of the compounds of this invention. Occasionally, the reactions may not be applicable as described to each compound included within the disclosed scope. The compounds for which this occurs will be readily recognized by those skilled in the art. In all such cases, either the reactions can be successfully performed by conventional modifications

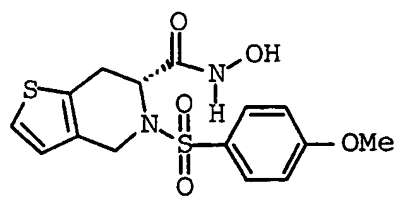
known to those skilled in the art, e.g., by appropriate protection of interfering groups, by changing to alternative conventional reagents, by routine modification of reaction conditions, and the like, or other reactions disclosed herein or otherwise conventional, will be applicable to the preparation of the corresponding compounds of this invention. In all preparative methods, all starting materials are known or readily prepared from known starting materials.

Prodrugs of the compounds of this invention are also contemplated by this invention. A prodrug is an active or inactive compound that is modified chemically through in vivo physicological action, such as hydrolysis, metabolism and the like, into a compound of this invention following adminstration of the prodrug to a patient. The suitability and techniques involved in making and using prodrugs are well known by those skilled in the art. For a general discussion of prodrugs involving esters see Svensson and Tunek Drug Metabolism Reviews 165 (1988) and Bundgaard Design of Prodrugs, Elsevier (1985). Examples of a masked carboxylate anion include a variety of esters, such as alkyl (for example, methyl, ethyl), cycloalkyl (for example, cyclohexyl), aralkyl (for example, benzyl, p-methoxybenzyl), and alkylcarbonyloxyalkyl (for example, pivaloyloxymethyl). Amines have been masked as arylcarbonyloxymethyl substituted derivatives which are cleaved by esterases in vivo releasing the free drug and formaldehyde (Bungaard J. Med. Chem. 2503 (1989)). Also, drugs containing an acidic NH group, such as imidazole, imide, indole and the like, have been masked with N-acyloxymethyl groups (Bundgaard Design of Prodrugs, Elsevier (1985)). Hydroxy groups have been masked as esters and ethers. EP 039,051 (Sloan and Little, 4/11/81) discloses Mannich-base hydroxamic acid prodrugs, their preparation and use.

Without further elaboration, it is believed that one skilled in the art can, using the preceding description, utilize the present invention to its fullest extent. The following preferred specific embodiments are, therefore, to be construed as merely illustrative, and not limitative of the remainder of the disclosure in any way whatsoever.

The following Examples illustrate the preparation of compounds of the present invention and intermediates useful in preparing the compounds of the present invention.

Example 1



Preparation of 5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6(R)-hyrdoxamic acid

Step A: 4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6(R)-carboxylic acid•HCl

Hydrogen chloride (1N, 0.3 ml, 2.9 mmole) was added into a mixture of 3-(2-thienyl)-D-alanine(500 mg, 2.9 mmole) and formaldehyde (37%, 0.72 ml, 8.8 mmole) in 5 ml of water. The reaction mixture was then heated to 90^{o}C for 3 hr. The solvent was removed under reduced pressure to obtain 4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6(R)-carboxylic acid hydrochloride salt (450 mg, 91%): ^{1}H NMR (D_2O) δ 7.50(d, 1H), 7.00(d, 1H), 4.60(d, 1H), 4.40(d, 1H), 4.38(dd, 1H), 3.62(dd, 1H), 3.39(dd, 1H).

Step B: methyl 4,5,6,7-tetrahydro-thieno[3,2-c] pyridine-6-carboxylate•HCl

Hydrogen chloride (gas) was bubbled through a solution of the carboxylic acid from step A (450 mg, 2.6 mmole) in 20

ml of methanol for 5 min (until ppt was dissolved). The reaction mixture was then refluxed at 80°C for 10 hr. Removal of the solvent under reduced pressure gave methyl 4,5,6,7-tetrahydro-thieno[3,2-c] pyridine-6-carboxylate hydrochloride salt (440 mg, 95%): ^{1}H NMR (D_2O) δ 10.5(bs, 2H), 7.20(s, 1H), 6.70(s, 1H), 4.30-4.60(bm, 3H), 3.85(s, 3H), 3.50(s, 1H), 3.40(s, 1H).

Step C: methyl 5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-carboxylate•HCl

A mixture of the methyl ester from step B (390 mg, 2 mmole), 4-dimethylaminopyridine (600 mg, 4.9 mmole) and 4-methoxybenzenesulfonyl chloride (529 mg, 2.6 mmole) in N,N-dimethylformamide (5 ml) was stirred at 25°C for 3 hr. The N,N-dimethylformamide was then removed under reduced pressure and the residue was subjected to column chromatography (ethylacetate:hexane, 1:1) yielding methyl 5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno [3,2-c]pyridine-6-carboxylate hydrochloride salt (390 mg, 54%): ^{1}H NMR ($CDCl_3$, 400 MHz), ppm: 7.78(d, 2H), 7.10(d, 1H), 6.80(d, 2H), 6.70(d, 1H), 5.10(d, 1H), 4.60(d, 1H), 4.30(d, 1H), 3.80(s, 3H),3.50(s, 3H), 3.30(d, 1H), 3.08(d, 1H).

Step D: 5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-carboxylic acid

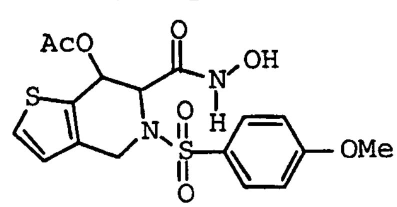
To a solution of the sulfonamide from step C (390 mg, 1.1 mmole) in tetrahydrofuran/water (2 ml each) at 25°C, was added lithium hydroxide (50 mg, 1.2 mmole) in one portion. The resulting reaction mixture was then stirred for 2 hr, followed by neutralization using 1N hydrochloric acid (1.2 ml). The combined mixture was then extracted with methylene chloride (30 ml), the methylene chloride fractions were washed with water (2x5 ml), dried (magnesium sulfate), and the solvent evaporated to obtain 5-(4-methoxyphenylsulfonyl)-

4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-carboxylic acid (200 mg, 51%): ^{1}H NMR ($CDCl_3$) δ 10.0(bs, 1H), 7.8(d, 2H), 7.1(d, 1H), 6.8(d, 2H), 6.6(d, 1H), 5.2(d, 1H), 4.6(d, 1H), 4.3(d, 1H), 3.8(s, 3H), 3.3(d, 1H), 3.0 (dd, 1H).

Step E: 5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-hydroxamic acid

A mixture of the acid from step D (93 mg, 0.26 mmole), hydroxyamine hydrochloride salt (31 mg, 0.44 mmole), N-methylmorpholine (0.15 ml, 1.3 mmole) and benzotriazol-1-yl-oxytripyrrolidinephosphonium hexafluorophosphate (Py-Bop) (232 mg, 0.44 mmole) in N,N-dimethylformamide was stirred at 25°C for 4 hr. The solvent was then removed under reduced pressure and the residue was subjected to column chromatography (5% methanol in methylene chloride) to yield 5-(4-methoxyphenyl ulfonyl)-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-hydroxamic acid (45 mg, 71%): ^{1}H NMR (MeOD-d_4) δ 7.70(d, 2H), 7.00(d, 1H), 6.80(d, 2H), 6.60(d, 1H), 4.80(bs, 1H), 4.60(d, 1H), 4.30(d, 1H), 3.80(s, 3H), 3.50(d, 1H), 2.60(bd, 1H); Mass Spec. Calcd. $C_{15}H_{16}O_5N_2S_2$ (M^+): 368, Found(M+1): 369.2 &(M+NH_4^+): 386.2.

Example 2



Preparation of 5-(4-methoxybenzenesulfonyl)-4,5,6,7-tetrahydro-7-acetoxy-thieno[3,2-c]pyridine-6-hydroxamic acid

Step A: threo ß-2-thienylserine

To a stirred solution of thiophene-2-carboxaldehyde (44.4g, 0.39mol) in absolute ethanol (80.0ml, 4.9M) was added glycine (14.8g, 0.20mol) at ambient temperature. The resulting suspension was cooled to $0^{o}C$, at which time a solution of potassium hydroxide (22.2g, 0.39mol) in absolute ethanol (120.0, 3.3M) was introduced in a dropwise manner. Upon complete addition, the reaction mixture was kept at $-10^{o}C$ for ninety minutes. The yellow solid which had precipitated during this time was collected via filtration and washed with ethanol. The solid was dissolved into water (70.0ml) and treated with glacial acetic acid (15.0ml). The resulting solution was stored at $-10^{o}C$ for eighteen hours. The precipitated product was collected via filtration to give 15.8g (43%) of threo ß-2-thienylserine.

Step B: 4,5,6,7-tetrahydro-7-hydroxy-thieno[3,2-c]pyridine-6-carboxylic acid hydrogen sulfate salt

To a stirred solution of threo ß-2-thienylserine (15.8g, 84.5mmol) in 0.25N sulfuric acid (140.0ml) was added 37% formaldehyde (45.0ml) at ambient temperature. The resulting mixture was stirred for three days after which time the product precipitated from solution. The solid was collected via filtration and washed with water (20ml) to give 5.2g (21%) of 4,5,6,7-tetrahydro-7-hydroxy-thieno[3,2-c]pyridine-6-carboxylic acid hydrogen sulfate salt.

Step C: 5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-7-hydroxy-thieno[3,2-c]pyridine-6-carboxylic acid

To a cooled ($0^{o}C$) suspension of 4,5,6,7-tetrahydro-7-hydroxy-thieno[3,2-c]pyridine-6-carboxylic acid hydrogen sulfate salt (0.77g, 2.59mmol) in 9% Na_2CO_3 (aq., 6.5ml) was slowly added a solution of 4-methoxybenzenesulfonyl chloride (0.53g, 2.59mmol) in 1,4-dioxane (6.5ml). Upon complete addition of the sulfonyl chloride, the cooling

bath was removed and the reaction was stirred at ambient temperature for one hour. The 1,4-dioxane was removed *in vacuo* and the remaining residue was diluted with water and ethyl acetate. The layers were separated. The aqueous phase was acidified to a pH of about 2 using 2M HCl and the product was extracted into ethyl acetate (twice). The combined organics were dried ($MgSO_4$), filtered and concentrated to give 0.44g (46%) of 5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-7-hydroxy-thieno[3,2-c]pyridine-6-carboxylic acid: ^1H NMR (DMSO-d_6) δ 3.75 (3H), 4.2-4.6 (2H), 4.7-5.0 (2H), 6.8 (1H), 7.2 (1H), 7.3 (1H), 7.7 (1H).

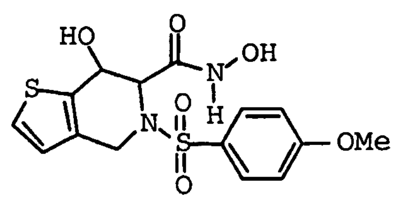
Step D: 5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-7-acetoxy-thieno[3,2-c]pyridine-6-carboxylic acid

To a stirred solution of 5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-7-hydroxy-thieno[3,2-c]pyridine-6-carboxylic acid (0.20g, 0.54mmol) in pyridine (5.0ml) was added acetic anhydride (60.0ml, 0.65mmol) at 0^oC under nitrogen atmosphere. The resulting mixture was stirred for one hour after which time it was quenched with water (115.0ml) and ethyl acetate (110.0ml). The layers were separated and the aqueous phase was extracted once more with ethyl acetate (110.0ml). The combined organics were dried ($MgSO_4$), filtered and concentrated to give the crude product. Purification via flash column chromatography (silica gel, 10% methanol/ethyl acetate) afforded 0.19g (86%) of 5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-7-acetoxy-thieno[3,2-c]pyridine-6-carboxylic acid: ^1H NMR ($CDCl_3$) δ 2.1 (3H), 3.8 (3H), 4.5-4.6 (2H), 5.2 (1H), 5.9 (1H), 6.7 (1H), 6.9 (2H), 7.2 (1H), 7.8 (2H), 8.1-8.7 (1H).

Step E: 5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-7-acetoxy-thieno[3,2-c]pyridine-6-hydroxamic acid

To a stirred solution of 5-(4-methoxybenzenesulfonyl)-4,5,6,7-tetrahydro-7-acetoxy-thieno[3,2-c]pyridine-6-carboxylic acid (0.19g, 0.46mmol) in dichloromethane (20.0ml) was added hydroxylamine hydrochloride (0.77g, 9.20mmol) at $0^{o}C$ under nitrogen. The resulting mixture was stirred for five minutes after which time it was treated with triethylamine (1.0ml, 7.2mmol) and PyBroP (Bromo-tris-pyrrolidino-phosphonium hexafluoro-phosphate, 0.32g, 0.69mmol). The reaction was stirred for five hours, during which time it had warmed to ambient temperature, and concentrated. The remaining residue was purified via column chromatography (silica gel, 5% methanol/ ethyl acetate) to give 5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydro-7-acetoxy-thieno[3,2-c]pyridine-6-hydroxamic acid: ^{1}H NMR ($CDCl_3$) δ 2.0 (3H), 3.7 (3H), 4.3-4.5 (2H), 4.8 (1H), 5.9 (1H), 6.6 (1H), 6.8 (2H), 7.1 (1H), 7.6 (2H), 10.7 (1H); Mass. Spec. 444.2 ($M+NH_4^+$).

Example 3

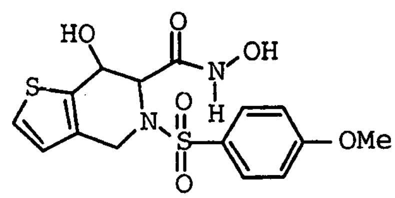


Preparation of 5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-7-hydroxy-thieno[3,2-c]pyridine-6-hydroxamic acid

To a stirred solution of 5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-7-acetoxy-thieno[3,2-c]pyridine-6-hydroxamic acid (18.0mg, 0.04mmol) in methanol (0.5ml, 0.08M) was added 20% potassium carbonate (aq., 0.5ml). After stirring at ambient temperature for 2.5 hours, the methanol was removed *in vacuo*. The remaining residue was diluted with water (5.0ml) and ethyl acetate (10.0ml). The layers were separated and the aqueous phase was extracted with ethyl acetate (three times

10.0ml). The combined organics were concentrated to give crude product. Purification via column chromatography (silica gel, 5% methanol/ethyl acetate) gave 5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-7-hydroxy-thieno[3,2-c]pyridine-6-hydroxamic acid as an off-white solid: ^{1}H NMR (DMSO) δ 3.8 (3H), 5.3-5.9 (4H), 6.8 (1H), 7.1 (2H), 7.4 (1H), 7.7 (2H), 8.5-8.8 (1H); Mass Spec. 385.2 (M+H), 402.0 ($M+NH_4^+$).

Example 4



Preparation of DL-cis 5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-7-hydroxy-thieno[3,2-c]pyridine-6-hydroxamic acid

Step A: DL-cis 2-(2-thienyl)serine

To a mechanically stirred solution of 2-thiophene arboxaldehyde (488.0g, 4.35mol) in absolute ethanol (900ml) was added glycine (98.5% purity, 165.8g, 2.17mol). The resulting suspension was cooled to 0°C. A solution of potassium hydroxide (87.9% purity, 277.6g, 4.35mol) in absolute ethanol (1.3L) was then added dropwise over 7.5 hours. During this time, the reaction became homogeneous and shortly after a precipitate formed. Upon complete addition of the ethanolic KOH solution, the reaction mixture was stirred for an additional 0.5 hours and placed in a freezer over night. The precipitated solid was collected *via* filtration and dissolved into water (1L). A sufficient volume of glacial acetic acid (about 230ml) was added to adjust the pH to 5.5. The resulting solution was cooled to induce the precipitation of the desired product. The solid was collected *via* filtration to give pure DL-cis

2-(2-thienyl)serine. The NMR(D_2O) spectrum was consistent with the proposed structure.

Step B: DL-cis 7-hydroxy-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-carboxylic acid

To a stirred suspension of DL-cis 2-(2-thienyl)-serine (116.0g, 0.62mol) in 0.25N sulfuric acid (1.2L) was added 37% formaldehyde (275.0ml) at ambient temperature. The reaction mixture became homogeneous. After three days, the precipitated product was collected *via* filtration. The pH of the filtrate was adjusted to 5.0-6.0 using 10N NaOH. The solid product was collected *via* filtration. The combined products were dried to give the desired product. The NMR (D_2O) spectrum was consistent with the proposed structure.

Step C: DL-cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-carboxylic acid

A suspension of DL-cis 7-hydroxy-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-carboxylic acid (35.0g, 175.9 mmol) in 9% sodium carbonate (440.0ml) was cooled to 0°C. To this suspension was added a solution of 4-methoxybenzenesulfonyl chloride (47.3g, 228.8mmol) in 1,4-dioxane (440ml) over one hour. Additional 9% sodium carbonate was added to maintain a pH=8-9. The reaction was allowed to stir over night during which time it had warmed to ambient temperature. The dioxane was removed and the remaining residue was diluted with water. This aqueous material was washed with ethyl acetate three times and then acidified to pH=2 using 2M HCl. The product was extracted with ethyl acetate (three times). The combined product extractions were washed successively with water and brine, then dried ($MgSO_4$). Filtration and concentration yielded DL-cis 7-hydroxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-carboxylic acid as a pink foam. The

NMR($CDCl_3$) spectrum was consistent with the proposed stucture.

Step D: DL-cis 7-acetoxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-carboxylic acid

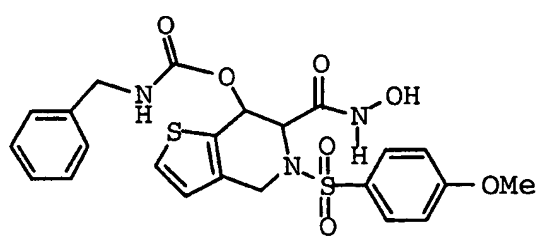
To a stirred solution of DL-cis 7-hydroxy-5-(4-methoxy phenylsulfonyl)-4,5,6,7-tetrahydro-thieno[3,2-c] pyridine-6-carboxylic acid (16.5g, 44.9mmol) in pyridine (440ml) was added acetic anhydride (5.0ml, 53.9mmol) at 0°C, under argon. After 1.5 hours, the reaction was diluted with cold water (100ml) then poured into ethyl acetate (800ml) and chilled 2M HCl (1L). The layers were separated and the organic was washed twice with chilled 2M HCl (1L) then twice with cold water (1L). The organic was then dried ($MgSO_4$), filtered and concentrated to yield DL-cis 7-acetoxy-5-(4-methoxy phenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-carboxylic acid. The NMR ($CDCl_3$) spectrum was consistent with the proposed structure.

Step E: DL-cis 7-Hydroxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

To a stirred solution of DL-cis 7-acetoxy-5-(4-methoxy phenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-carboxylic acid (5.3g, 12.9mmol) in dichloromethane (60ml) was added oxalyl chloride (12.9ml of a 2M dichloromethane solution, 25.8mmol) at ambient temperature, under argon. One drop of DMF was added to catalyze the formation of the acid chloride intermediate. After stirring for 1.5 hours, the reaction was cooled to 0°C. A solution of hydroxylamine hydrochloride (3.6g, 51.6mmol) and diisopropylethylamine (13.5ml, 77.4mmol) in THF (50ml) and water (4ml) was then carefully added in a dropwise manner. Upon complete addition, the reaction mixture was stirred at

ambient temperature over night and then poured into water and dichloromethane. The layers were separated and the aqueous phase was extracted once with dichloromethane. The combined organics were washed twice with 0.5M HCl (50ml) and dried ($MgSO_4$). Filtration and concentration gave a brown foam which was dissolved into methanol (100ml) and diluted with 5% K_2CO_3 (100ml). After fifteen minutes, the reaction mixture was concentrated to low volume. The remaining aqueous was poured into 0.5M HCl (pH=1) and dichloromethane. The layers were separated and the aqueous phase was extracted twice with dichloromethane. The combined organics were allowed to stand at ambient temperature. DL-cis 7-Hydroxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro thieno[3,2-c]pyridine-6-hydroxamic acid precipitated as an off-white solid which was collected *via* filtration. The NMR (DMSO) spectrum was consistent with the proposed structure.

Example 5



Preparation of DL-cis 7-(N-benzylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid

Step A: DL-cis 7-(N-benzylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid

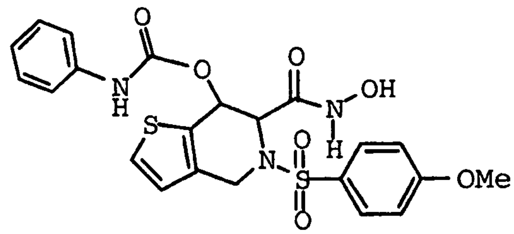
To a stirred solution of DL-cis 7-hydroxy-5-(4-methoxy phenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-carboxylic acid (88.0mg, 0.24mmol) in dry DMF (1.5ml) was added copper (I) bromide (34.0mg, 0.24mmol) at ambient temperature. After stirring for five minutes,

benzyl isocyanate (29.0ul, 0.24mmol) was introduced *via* syringe. The resulting mixture was stirred for five minutes and then diluted with water (40ml). The product was extracted into ethyl acetate (twice). The combined organics were washed with dilute HCl (aq.) and dried ($MgSO_4$). Filtration and concentration gave DL-cis 7-(N-benzylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid which was used without further purification. NMR($CDCl_3$) was consistent with the proposed structure.

Step B: DL-cis-7-(N-benzylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid

To a stirred solution of DL-cis 7-(N-benzylamino carbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid (0.11g, 0.22mmol) in anhydrous dichloromethane was added oxalyl chloride (0.22ml, 0.44mmol) at 0°C, under argon. One drop of DMF was added to catalyze the formation of the acid chloride intermediate. After stirring for two hours, the mixture had warmed to ambient temperature. The reaction was again cooled to 0°C. A solution of hydroxylamine hydrochloride (61.0mg, 0.88mmol) and diisopropylethylamine (0.23ml, 1.32mmol) in THF (0.15ml) and water (1 drop) was added *via* syringe (dropwise). The resulting mixture was stirred for four hours at ambient temperature and poured into water and dichloromethane. The layers were separated and the organic phase was washed with dilute HCl (aq.) and dried ($MgSO_4$). Filtration and concentration gave the crude product. Purification *via* preparative TLC (silica gel, 10% methanol/dichloromethane) afforded pure DL-cis 7-(N-benzylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid. NMR (DMSO) and MS (M-1 = 516) were consistent with the proposed structure.

Example 6



Preparation of DL-cis 7-(N-phenylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid

Step A: DL-cis 7-(N-phenylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid

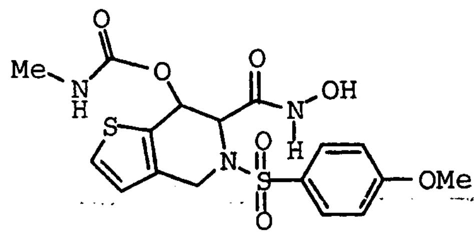
Utilizing phenyl isocyanate, DL-cis 7-(N-phenylamino carbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid was prepared from DL-cis 7-hydroxy-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-carboxylic acid in the same manner as DL-cis 7-(N-benzylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid. DL-cis 7-(N-phenylaminocarbonyloxy)-5-(4-methoxy phenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid was purified *via* flash column chromatography (silica gel, 20% ethyl acetate in dichloromethane, and 10% methanol in dichloromethane). NMR ($CDCl_3$) was consistent with the proposed structure.

Step B: DL-cis 7-(N-phenylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid

DL-cis 7-(N-phenylaminocarbonyloxy)-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid was prepared in the same manner as DL-cis 7-(N-benzylaminocarbonyloxy)-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-

hydroxamic acid. DL-cis 7-(N-phenylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid was purified *via* preparative TLC (silica gel, 5% methanol in dichloromethane). NMR (DMSO) and MS (M-1 = 502) were consistent with the proposed structure.

Example 7



Preparation of DL-cis 7-(N-methylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid

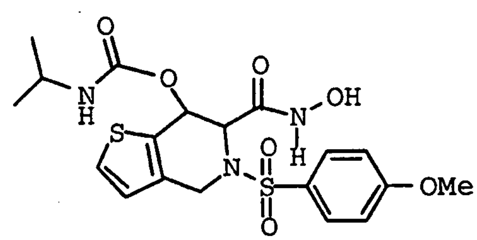
Step A: DL-cis 7-(N-methylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid

Utilizing methyl isocyanate, DL-cis 7-(N-methylamino carbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid was prepared from DL-cis 7-hydroxy-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-carboxylic acid in the same manner as DL-cis 7-(N-benzylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid. DL-cis 7-(N-methylaminocarbonyloxy)-5-(4-methoxy phenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid was purified *via* flash column chromatography (silica gel, 15% methanol in dichloromethane). NMR ($CDCl_3$) was consistent with the proposed structure.

Step B: DL-cis 7-(N-methylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid

DL-cis 7-(N-methylaminocarbonyloxy)-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid was prepared in the same manner as DL-cis 7-(N-benzylaminocarbonyloxy)-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid. DL-cis 7-(N-methylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid was purified *via* preparative TLC (silica gel, 5% methanol in dichloromethane). NMR (DMSO) and MS (M-1 = 440) were consistent with the proposed structure.

Example 8



Preparation of DL-cis 7-(N-isopropylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid

Step A: DL-cis 7-(N-isopropylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid

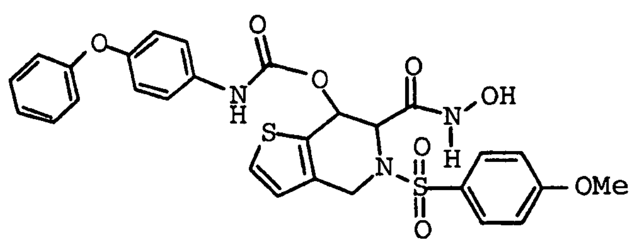
Utilizing isopropyl isocyanate, DL-cis 7-(N-isopropyl aminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid was prepared from DL-cis 7-hydroxy-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-carboxylic acid in the same manner as DL-cis 7-(N-benzylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid. DL-cis 7-(N-isopropylaminocarbonyloxy)-5-(4-

methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid was purified *via* flash column chromatography (silica gel, 20% ethyl acetate in dichloromethane, and 10% methanol in dichloromethane). NMR ($CDCl_3$) was consistent with the proposed structure.

Step B: DL-cis 7-(N-isopropylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid

DL-cis 7-(N-isopropylaminocarbonyloxy)-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid was prepared in the same manner as DL-cis 7-(N-benzylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid. DL-cis 7-(N-isopropylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid was purified *via* preparative TLC (silica gel, 10% methanol in dichloromethane). NMR (DMSO) and MS (M+1 = 470) were consistent with the proposed structure.

Example 9



Preparation of DL-cis 7-(N-(4-phenoxyphenyl)amino carbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid

Step A: DL-cis 7-(N-(4-phenoxyphenyl)aminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid

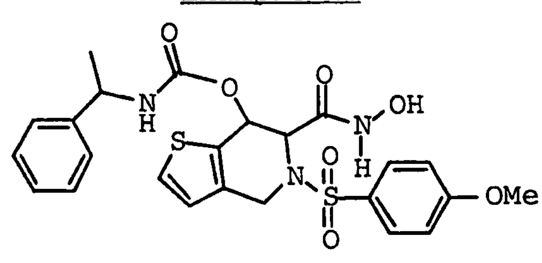
Utilizing 4-phenoxyphenyl isocyanate, DL-cis 7-(N-(4-phenoxyphenyl)aminocarbonyloxy)-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-

carboxylic acid was prepared from DL-cis 7-hydroxy-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-carboxylic acid in the same manner as DL-cis 7-(N-benzylaminocarbonyloxy)-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid. DL-cis 7-(N-(4-phenoxyphenyl)amino carbonyloxy)-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid was purified *via* flash column chromatography (silica gel, 20% ethyl acetate in dichloromethane, and 10% methanol in dichloromethane).

Step B: DL-cis 7-(N-(4-phenoxyphenyl)aminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid

DL-cis 7-(N-(4-phenoxyphenyl)aminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid was prepared in the same manner as DL-cis 7-(N-benzylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid. DL-cis 7-(N-(4-phenoxy phenyl)aminocarbonyloxy)-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid was purified *via* preparative TLC (silica gel, 10% methanol in dichloromethane). NMR (DMSO) and MS (M+1 = 596) were consistent with the proposed structure.

Example 10



Preparation of DL-cis 7-(N-(1-phenylethyl)amino carbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid

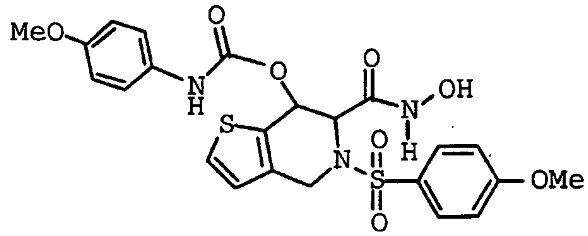
Step A: DL-cis 7-(N-(1-phenylethyl)aminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid

Utilizing 1-phenylethyl isocyanate, DL-cis 7-(N-(1-phenylethyl)aminocarbonyloxy)-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid was prepared from DL-cis 7-hydroxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-carboxylic acid in the same manner as DL-cis 7-(N-benzylaminocarbonyloxy)-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid. DL-cis 7-(N-(1-phenylethyl)amino carbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid was purified *via* flash column chromatography (silica gel, 15% ethyl acetate in dichloromethane, and 10% methanol in dichloromethane).

Step B: DL-cis 7-(N-(1-phenylethyl)aminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid

DL-cis 7-(N-(1-phenylethyl)aminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid was prepared in the same manner as DL-cis 7-(N-benzylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid. DL-cis 7-(N-(1-phenyl ethyl)aminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid was purified *via* preparative TLC (silica gel, 5% methanol in dichloromethane). NMR (DMSO) and MS (M+1 = 532) were consistent with the proposed structure.

Example 11



Preparation of DL-cis 7-(N-(4-methoxyphenyl)amino carbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid

Step A: DL-cis 7-(N-(4-methoxyphenyl)aminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid

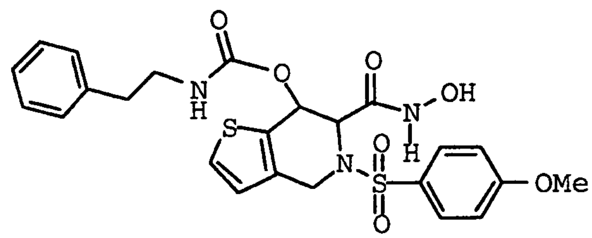
Utilizing 4-methoxyphenyl isocyanate, DL-cis 7-(N-(4-methoxyphenyl)aminocarbonyloxy)-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid was prepared from DL-cis 7-hydroxy-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c] pyridine-6-carboxylic acid in the same manner as DL-cis 7-(N-benzylaminocarbonyloxy)-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid. DL-cis 7-(N-(4-methoxyphenyl)amino carbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid was purified *via* flash column chromatography (silica gel, 15% ethyl acetate in dichloromethane, and 10% methanol in dichloromethane).

Step B: DL-cis 7-(N-(4-methoxyphenyl)aminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid

DL-cis 7-(N-(4-methoxyphenyl)aminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid was prepared in the same manner as DL-cis 7-(N-benzylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid. DL-cis 7-(N-(4-methoxy

phenyl)aminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid was purified *via* preparative TLC (silica gel, 5% methanol in dichloromethane). NMR (DMSO) and MS (M+1 = 534) were consistent with the proposed structure.

Example 12



Preparation of DL-cis 7-(N-(phenethyl)aminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid

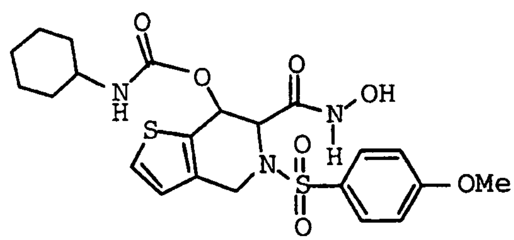
Step A: DL-cis 7-(N-(phenethyl)aminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid

Utilizing phenethyl isocyanate, DL-cis 7-(N-(phenethyl) aminocarbonyloxy)-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid was prepared from DL-cis 7-hydroxy-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-carboxylic acid in the same manner as DL-cis 7-(N-benzylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid. DL-cis 7-(N-(phenethyl)aminocarbonyloxy)-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid was purified *via* flash column chromatography (silica gel, 15% ethyl acetate in dichloromethane, and 10% methanol in dichloromethane).

Step B: DL-cis 7-(N-(phenethyl)aminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid

DL-cis 7-(N-(phenethyl)aminocarbonyloxy)-5-(4-methoxy phenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid was prepared in the same manner as DL-cis 7-(N-benzylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid. DL-cis 7-(N-(phenethyl) aminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid was purified *via* preparative TLC (silica gel, 5% methanol in dichloromethane). NMR (DMSO) and MS (M+1 = 532) were consistent with the proposed structure.

Example 13



Preparation of DL-cis 7-(N-cyclohexylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid

Step A: DL-cis 7-(N-cyclohexylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid

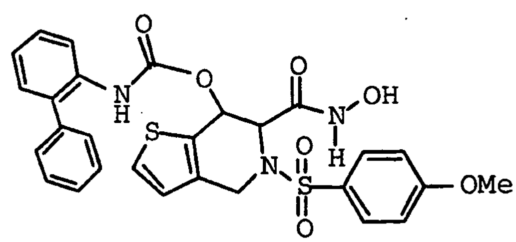
Utilizing cyclohexyl isocyanate, DL-cis 7-(N-cyclohexyl aminocarbonyloxy)-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid was prepared from DL-cis 7-hydroxy-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-carboxylic acid in the same manner as DL-cis 7-(N-benzylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid. DL-cis 7-(N-cyclohexylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid was purified *via* flash

column chromatography (silica gel, 10% ethyl acetate in dichloromethane, and 8% methanol in dichloromethane).

Step B: DL-cis 7-(N-cyclohexylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid

DL-cis 7-(N-cyclohexylaminocarbonyloxy)-5-(4-methoxy phenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid was prepared in the same manner as DL-cis 7-(N-benzylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid. DL-cis 7-(N-cyclohexyl aminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid precipitated from dichloromethane. NMR (DMSO) and MS (M-1 = 508) were consistent with the proposed structure.

Example 14



Preparation of DL-cis 7-(N-(2-biphenyl)aminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid

Step A: DL-cis 7-(N-(2-biphenyl)aminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid

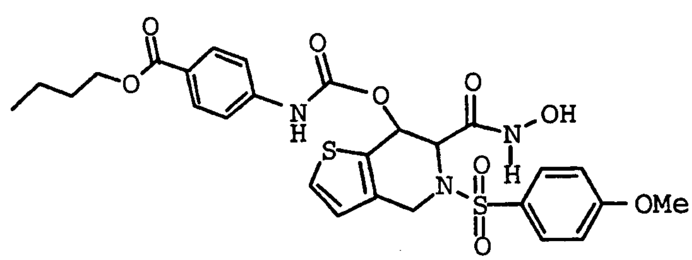
Utilizing 2-biphenylisocyanate, DL-cis 7-(N-(2-biphenyl) aminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid was prepared from DL-cis 7-hydroxy-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-carboxylic acid in the same manner as DL-cis 7-(N-

benzylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid. DL-cis 7-(N-(2-biphenyl)aminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid was purified *via* flash column chromatography (silica gel, 10% ethyl acetate in dichloromethane, and 8% methanol in dichloromethane).

Step B: DL-cis 7-(N-(2-biphenyl)aminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid

DL-cis 7-(N-(2-biphenyl)aminocarbonyloxy)-5-(4-methoxy phenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid was prepared in the same manner as DL-cis 7-(N-benzylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid. DL-cis 7-(N-(2-biphenyl) aminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid was purified *via* preparative TLC (silica gel, 5% methanol in dichloromethane). NMR (DMSO) and MS (M-1 = 578) were consistent with the proposed structure.

Example 15



Preparation of DL-cis 7-(N-(4-butoxycarbonylphenyl) aminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid

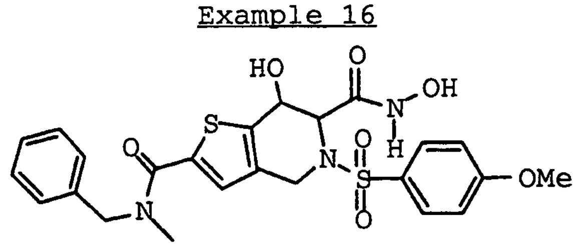
Step A: DL-cis 7-(N-(4-butoxycarbonylphenyl)amino carbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid

Utilizing 4-butoxycarbonylphenyl isocyanate, DL-cis 7-(N-(4-butoxycarbonylphenyl)aminocarbonyloxy)-5-(4-methoxy phenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid was prepared from DL-cis 7-hydroxy-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-carboxylic acid in the same manner as DL-cis 7-(N-benzylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid. DL-cis 7-(N-(4-butoxy carbonylphenyl)aminocarbonyloxy)-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-carboxylic acid was purified *via* flash column chromatography (silica gel, 10% ethyl acetate in dichloromethane, and 8% methanol in dichloromethane).

Step B: DL-cis 7-(N-(4-butoxycarbonylphenyl)amino carbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid

DL-cis 7-(N-(4-butoxycarbonylphenyl)aminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid was prepared in the same manner as DL-cis 7-(N-benzylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid. DL-cis 7-(N-(4-butoxy carbonylphenyl)aminocarbonyloxy)-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid was purified *via* preparative TLC (silica gel, 5% methanol in dichloromethane). NMR (CD_3OD) and MS (M-1 = 602) were consistent with the proposed structure.

Example 16



Preparation of cis-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-2-(N-benzyl-N-methylaminocarbonyl)-4,5,6,7-tetrahydro thieno-[3,2-c]-pyridinyl-6-hydroxamic acid

Step A: cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-6-(methoxycarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine

To a solution of cis-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-7-hydroxy-thieno[3,2-c]pyridine-6-carboxylic acid (369 mg, 1.0 mmole) in methanol (5.0 mL) at 0°C was dropwise added (trimethylsilyl)diazomethane (2.0 M solution in hexane, 1.0 mL, 2.0 mmole). The reaction mixture was then stirred at that temperature for 30 min, followed by stirring at 25°C for another 30 min. The solvent was removed by reduced pressure and the residue was subjected to chromatographic purification (35% EtOAc in hexane) giving pure cis-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-6-(methoxy carbonyl)-4,5,6,7-tetrahydrothieno [3,2-c]pyridine: White solid; TLC, Rf = 0.5 (40% EtOAc in hexane); ^{1}H NMR ($CDCl_3$) δ 3.45(s, 3H), 3.82(s, 3H), 4.50(dd, 2H), 5.20(bd, 1H), 5.25(bs, 1H), 6.78(d, 1H), 6.98(d, 2H), 7.22(d, 1H), 7.80(d, 2H); MS: Calcd. $C_{16}H_{17}NO_6S_2$ (M^+) = 383, Found $(M+H)^+$ = 384.2, $(M+NH_4)^+$ = 401.2.

Step B: cis-2-iodo-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-6-(methoxycarbonyl)-4,5,6,7-tetrahydrothieno [3,2-c]pyridine

To a solution of cis-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-6-(methoxycarbonyl)-4,5,6,7-tetrahydrothieno [3,2-c]pyridine (383 mg, 1.0 mmol) in CCl_4 (5.0 mL) and CH_2Cl_2 (1.0 mL) at 25°C was added I_2 (140 mg, 0.55 mmol) in one portion, followed by addition of bis(trifluoro acetoxy)iodobenzene (237 mg, 0.55 mmol). The reaction mixture was allowed to stir at that temperature for 3 hr. The solvent was removed under reduced pressure and the residue was subjected to chromatographic

purification (30% EtOAc in hexane) to obtain pure cis-2-iodo-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-6-(methoxy carbonyl)-4,5,6,7-tetrahydro thieno[3,2-c]pyridine: White solid; TLC, Rf = 0.52 (40% EtOAc in hexane); ^{1}H NMR ($CDCl_3$) δ 3.50(s, 3H), 3.91(s, 3H), 5.00(bt, 1H), 5.15(d, 1H), 6.85(s, 1H), 6.92(d, 2H), 7.78(d, 2H); MS: Calcd. $C_{16}H_{16}NO_6S_2I$(M+) = 509, Found $(M+H)^+$ = 509.8, $(M+NH_4)^+$ = 526.6.

Step C: cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-benzyl-N-methylaminocarbonyl)-6-(methoxycarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine

A mixture of 2-iodo-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-6-(methoxycarbonyl)-4,5,6,7-tetrahydrothieno [3,2-c]pyridine (509 mg, 1.0 mmole), N-methyl-N-benzyl amine (3.0 mL) and nickel tetracarbonyl (0.39 mL, 3 mmole) was stirred well and heated at 55°C under argon atomsphere for 2 hr. The reaction mixture was then directly subjected to chromatographic purification (60% EtOAc in hexane) giving pure cis-7-hydroxy-5-(4-methoxy phenylsulfonyl)-2-(N-benzyl-N-methylaminocarbonyl)-6-(methoxycarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine: Oil; TLC, Rf = 0.25(60% EtOAc in hexane); ^{1}H NMR ($CDCl_3$) δ 3.05(bs, 3H), 3.45(s, 3H), 3.84(s, 3H), 4.28(bdd, 2H), 4.90(bs, 2H), 5.10(bs, 1H), 5.20(bs, 1H), 5.23(bs, 1H), 6.98(d, 2H), 7.22(s, 1H), 7.36(m, 3H), 7.70(d, 2H), 7.80(d, 2H); MS: Calcd. $C_{25}H_{26}N_2O_7S_2$(M^+) = 530, Found $(M+H)^+$ = 531.3, $(M+NH_4)^+$ = 548.0.

Step D: cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-benzyl-N-methylaminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-carboxylic acid

To a solution of cis-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-2-(N-benzyl-N-methylaminocarbonyl)-6-(methoxy carbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine (530 mg, 1.0 mmole) in THF (4.0 mL) and H_2O (4.0 mL) at 25°C was added $LiOH \cdot H_2O$ (124 mg, 3.0 mmole) in one portion.

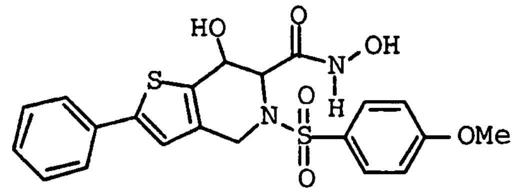
The reaction mixture was allowed to stir at that temperature for 1 hr, followed by quenching the reaction with 1N HCl (3.0 mL, 3.0 mmole). Dilution with CH_2Cl_2 (100 mL), washing with H_2O (2x10 mL), dried ($MgSO_4$), filtered and finally, removal of the solvent under reduced pressure gave crude cis-7-hydroxy-5-(4-methoxy phenylsulfonyl)-2-(N-benzyl-N-methylaminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-carboxylic acid which was subjected to the next reaction without further purification.

Step E: cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-benzyl-N-methylaminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid

To a solution of cis-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-2-(N-benzyl-N-methylaminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-carboxylic acid (516 mg, 1.0 mmole) in DMF (5.0 mL) at 25°C was sequentially added hydroxylamine hydrochloride (209 mg, 3.0 mmole), N,N-diisopropylethylamine (0.7 mL, 4.0 mmole) and Py-BroP (700 mg, 1.5 mmol). The reaction mixture was then stirred at that temperature for 2 hr. Standard aqueous work up (extraction with CH_2Cl_2) followed by chromatographic purification (5% MeOH in EtOAc) gave pure cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-benzyl-N-methylaminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid: White solid; TLC, Rf = 0.5 (10% MeOH in EtOAc); ^1H NMR (acetone-d_6) δ 3.10(bs, 3H), 3.85(s, 3H), 4.55(bs, 2H), 4.78(bs, 2H), 4.80(s, 1H), 5.05(s, 1H), 7.00(d, 2H), 7.28(m, 6H), 7.82(d, 2H), 10.30(bs,1H); MS: Calcd. $C_{24}H_{25}N_3O_7S_2$ (M^+) = 531, Found $(M+H)^+$ = 532, $(M+NH_4)^+$ = 549.

Example 17

Preparation of cis-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-2-phenyl-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid



Step A: cis-2-iodo-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-carboxylic acid

cis-2-Iodo-7-hydroxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-carboxylic acid was prepared from cis-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-carboxylic acid in the same manner as cis-2-iodo-7-hydroxy-5-(4-methoxy phenylsulfonyl)-6-(methoxy carbonyl)-4,5,6,7-tetrahydro thieno[3,2-c]pyridine: Brown solid; TLC, Rf = 0.5 (20% MeOH in CH_2Cl_2); 1H NMR (DMSO-d_6) δ 3.82(s, 3H), 4.30(bs, 2H), 4.36(bd, 1H), 4.50(bd, 2H), 6.82(s, 1H), 7.02(d, 2H), 7.76(d, 2H); MS: Calcd. $C_{15}H_{14}NO_6S_2I(M^+)$ = 495, Found $(M-H)^-$ = 494.

Step B: cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-phenyl-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-carboxylic acid

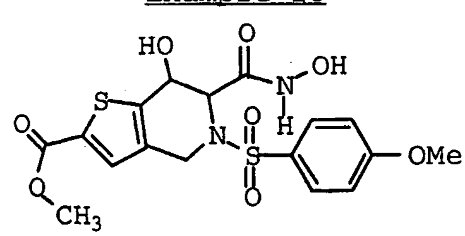
To a solution of tributylphenyl tin (1.1 g, 3.0 mmole) in THF at -78°C was dropwise added nBuLi (2M, 1.5 mL, 3.0 mmole). The reaction mixture was then stirred at that temperature for 10 min, followed by an addition of $ZnCl_2$ (0.5M, 6.0 mL, 3.0 mmole). The reaction mixture was then allowed to slowly warm up to 25°C and was stirred at that temperature for another 10 min. The above Zn-reagent was then added into a mixture of cis-2-iodo-7-hydroxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-carboxylic acid (495 mg, 1.0 mmole) and tetrakis(triphenylphosphine)palladium (0) (58 mg, 0.05 mmole) in THF (20 mL) at 25°C and let the mixture stir at that temperature for another 1 hr.

Standard aqueous work up, extraction with CH_2Cl_2, removal of the solvent, and finally, chromatographic purification (5% MeOH in CH_2Cl_2) gave pure cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-phenyl-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-carboxylic acid: White solid; TLC, Rf = 0.5 (10% MeOH in CH_2Cl_2); ^{1}H NMR (MeOD-d_4) δ 3.72(s, 3H), 4.30(dd, 2H), 4.50(bs, 1H), 4.68(bs, 1H), 6.90(m, 3H), 7.10(s, 1H), 7.25(m, 1H), 7.50(m, 2H), 7.88(m, 2H); MS: Calcd. $C_{21}H_{19}NO_6S_2(M^+)$ = 445, Found $(M-H)^-$ = 444.2.

Step C: cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-phenyl-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid

cis-7-Hydroxy-5-(4-methoxyphenylsulfonyl)-2-phenyl-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid was prepared from cis-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-2-phenyl-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-carboxylic acid in the same manner as cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-benzyl-N-methylaminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid: White solid; TLC, Rf = 0.5 (5% MeOH in CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 3.82(s, 3H), 4.55(dd, 2H), 5.05(bt, 2H), 6.85(s, 1H), 6.92(b, 2H), 7.32(t, 2H), 7.50(d, 2H), 7.80(d, 2H); MS: Calcd. $C_{21}H_{20}N_2O_6S_2(M^+)$ = 460, Found $(M-H)^-$ = 459.2.

Example 18



Preparation of cis-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-2-(methoxycarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid

Step A: cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2,6-bis(methoxycarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c] pyridine

Carbon monoxide was bubbled through a mixture of cis-2-iodo-7-hydroxy-5-(4-methoxyphenylsulfonyl)-6-(methoxy carbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine (509 mg, 1.0 mmole), triethyl amine (0.15 mL, 1.1 mmole) and palladium acetate (4.5 mg, 0.02 mmole) in methanol (10 mL) for 10 min. Subsequently, the reaction mixture was then heated at 70°C for 5 hr. The solvent was removed under reduced pressure and the residue was subjected to chromatographic purification (40% EtOAc in hexane) to obtain pure cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2,6-bis(methoxycarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c] pyridine: Oil; TLC, Rf = 0.45 (50% EtOAc in hexane); ^1H NMR ($CDCl_3$) δ 3.50(s, 3H), 3.84(s, 3H), 3.85(s, 3H), 4.06(d, 1H), 4.08 and 4.62(dd, 2H), 5.20(d, 1H), 6.92(d, 2H), 7.21(s, 1H), 7.78(d, 2H); MS: Calcd. $C_{18}H_{19}NO_8S_2$ (M^+) = 441, Found $(M+H)^+$ = 442.2, $(M+NH_4)^+$ = 459.0.

Step B: cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(methoxycarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c] pyridine-6-carboxylic acid

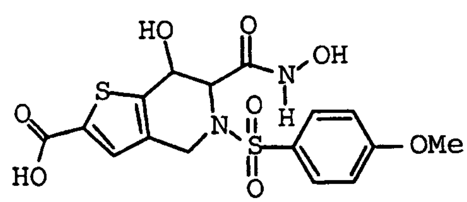
To a suspension of cis-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-2,6-bis(methoxycarbonyl)-4,5,6,7-tetrahydro thieno[3,2-c]pyridine (441 mg, 1.0 mmole) in THF (5 mL) and H_2O (5 mL) was added $LiOH\text{-}H_2O$ (46 mg, 1.1 mmole) in one portion. The reaction mixture was allowed to stir at that temperature for 1 hr until which time the starting material was consumed. The reaction was then quenched with 1N HCl (1.1 mL, 1.1 mmole) to pH = 7. The solvents were removed under reduced pressure and the residue was subjected to chromatographic purification (20% MeOH in CH_2Cl_2) to give pure cis-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-2-(methoxycarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-carboxylic acid:

White solid; TLC, Rf = 0.3 (20% MeOH in CH_2Cl_2); ^1H NMR (DMSO-d_6) δ 3.75(s, 3H), 3.78(s, 3H), 4.37(dd, 2H), 4.38(bd, 2H), 4.52(bd, 2H), 7.00(d, 2H), 7.50(s, 1H), 7.78(d, 2H); MS: Calcd. $C_{17}H_{17}NO_8S_2$ (M^+) = 427, Found $(M-H)^-$ = 426.2, $(M+NH_4)^+$ = 445.2.

<u>Step C: cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(methoxycarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c] pyridine-6-hydroxamic acid</u>

cis-7-Hydroxy-5-(4-methoxyphenylsulfonyl)-2-(methoxy carbonyl)-4,5,6,7-tetrahydrothieno[3,2-c] pyridine-6-hydroxamic acid was prepared from cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(methoxycarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c] pyridine-6-carboxylic acid in the same manner as cis-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-2-(N-benzyl-N-methylamino carbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid: White solid; TLC, Rf = 0.4 (10% MeOH in CH_2Cl_2); 1H NMR (MeOD-d_4) δ 3.82(s, 3H), 4.50(dd, 2H), 4.75(bs, 1H), 4.86(bs, 1H), 6.96(d, 2H), 7.50(s, 1H), 7.80(d, 2H); MS: Calcd. $C_{17}H_{18}N_2O_8S_2$ (M^+) = 442, Found $(M-H)^-$ = 441.2.

<u>Example 19</u>

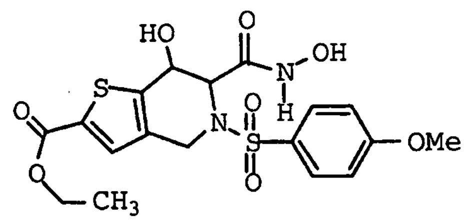


<u>Preparation of cis-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-2-carboxy-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid</u>

To a suspension of cis-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-2-(methoxycarbonyl)-4,5,6,7-tetrahydrothieno [3,2-c]pyridine-6-hydroxamic acid (442 mg, 1.0 mmole) in THF (5 mL) and H_2O (5 mL) at 25°C was added $LiOH{\cdot}H_2O$ (84 mg, 2.0 mmole) in one portion. The reaction mixture was allowed to stir at that temperature for 1 hr at which

time the starting material was consumed. The reaction was then quenched with 1N HCl (2 mL, 2.0 mmole) to pH 7. The solvents were removed under reduced pressure and the residue was subjected to chromatographic purification (40% MeOH in CH_2Cl_2) yielding pure cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-carboxy-4,5,6,7-tetrahydro thieno-[3,2-c]-pyridine-6-hydroxamic acid: White solid; TLC, Rf = 0.3 (40% MeOH in CH_2Cl_2); ^1H NMR (DMSO-d_6) δ 3.78(s, 3H), 4.20(bs, 1H), 4.40(dd, 2H), 4.78(bs, 1H), 6.20(bs, 1H), 6.92(bs, 1H), 7.02(bd, 2H), 7.80(d, 2H), 8.80(bs, 1H), 11.00(bs, 1H); MS: Calcd. $C_{16}H_{16}N_2O_8S_2$ (M^+) = 428, Found $(M-H)^-$ = 427.2, $(M+NH_4)^+$ = 446.

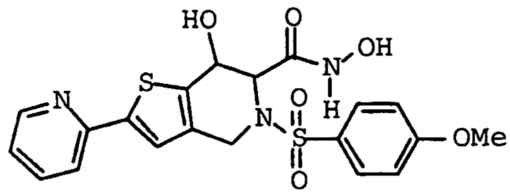
Example 20



Preparation of cis-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-2-(ethoxycarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid

Utilizing ethanol, cis-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-2-(ethoxycarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid was prepared from cis-2-iodo-7-hydroxy-5-(4-methoxyphenylsulfonyl)-6-(methoxy carbonyl)-4,5,6,7-tetrahydrothieno[3,2-c] pyridine in the same manner as cis-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-2-(methoxycarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid: White solid; TLC, Rf = 0.41 (10% MeOH in CH_2Cl_2); ^1H NMR (DMSO-d_6) δ 1.30(t, 3H), 3.81(s, 1H), 4.10(q, 2H), 4.30(dd, 2H), 4.55(d, 1H), 4.90(d, 1H), 7.10(d, 2H), 7.50(s, 1H), 7.72(d, 1H), 7.90(bs, 1H); MS: Calcd. $C_{18}H_{20}N_2O_8S_2(M^+)$ = 456, Found: $(M-H)^-$ = 455.2, $(M+H)^+$ = 457.2, $(M+NH_4)^+$ = 474.2.

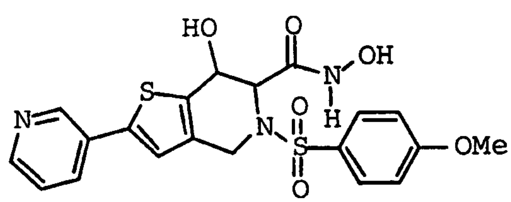
Example 21



Preparation of cis-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-2-(2-pyridyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid

Utilizing bromo(2-pyridinyl)zinc, cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(2-pyridyl)-4,5,6,7-tetrahydro thieno-[3,2-c]-pyridinyl-6-hydroxamic acid was prepared from cis-2-iodo-7-hydroxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-carboxylic acid in the same manner as cis-7-hydroxy-5-(4-methoxy phenylsulfonyl)-2-(2-phenyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid: White solid; TLC, Rf = 0.70(10% MeOH in CH_2Cl_2); ^1H NMR (acetone-d_6) δ 3.90(s, 3H), 4.60(dd, 2H), 4.95(bd, 1H), 5.00(bd, 1H), 7.05(d, 2H), 7.24(m, 1H), 7.45(s, 1H), 7.76(m, 2H), 7.85(d, 2H), 8.50(d, 1H); MS: Caldc. $C_{20}H_{19}N_3O_6S_2(M^+)$ = 461, Found: $(M+H)^+$ = 462.0.

Example 22

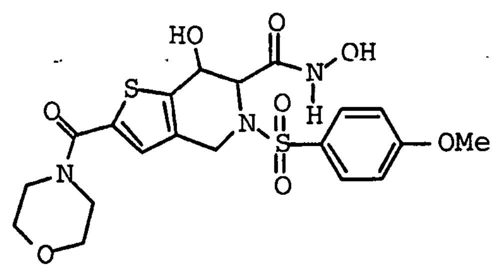


Preparation of cis-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-2-(3-pyridyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid

Utilizing bromo(3-pyridinyl)zinc, cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(3-pyridyl)-4,5,6,7-tetrahydro thieno-[3,2-c]-pyridinyl-6-hydroxamic acid was prepared from cis-2-iodo-7-hydroxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-carboxylic

acid in the same manner as cis-7-hydroxy-5-(4-methoxy phenylsulfonyl)-2-(2-pyridyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid: White solid; TLC, Rf = 0.55(10% MeOH in CH_2Cl_2); ^{1}H NMR (acetone-d_6) δ 3.92(s, 3H), 4.60(dd, 2H), 4.90(d, 1H), 5.00(bt, 1H), 6.10(d, 1H), 7.10(d, 2H), 7.28(s, 1H), 7.40(dd, 1H), 7.98(d, 1H), 8.20(bs, 1H), 8.52(d, 1H), 8.84(s, 1H), 10.35(bs, 1H); 85(d, 2H), 8.50(d, 1H); MS: Caldc. $C_{20}H_{19}N_3O_6S_2(M^+)$ = 461, Found: $(M+H)^+$ = 462.2.

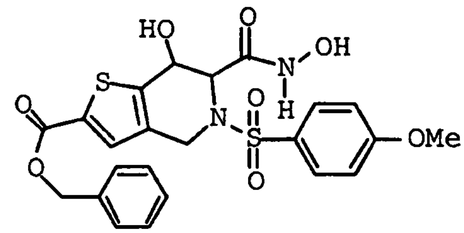
Example 23



Preparation of cis-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-2-(4-morpholinocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid

Utilizing morpholine, cis-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-2-(4-morpholinocarbonyl)-4,5,6,7-tetrahydro thieno-[3,2-c]-pyridine-6-hydroxamic acid was prepared from cis-2-iodo-7-hydroxy-5-(4-methoxyphenylsulfonyl)-6-(methoxycarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c] pyridine in the same manner as cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-benzyl-N-methylamino carbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid: White solid; TLC, Rf = 0.40(10% MeOH in CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 3.70(bs, 8H), 3.90(s, 3H), 4.40(dd, 2H), 4.75(bs, 1H), 4.90(bs, 1H), 5.85(bs, 1H), 6.90(d, 2H), 6.95(s, 1H), 7.80(d, 2H), 9.75(bs, 1H); MS: Caldc. $C_{20}H_{23}N_3O_8S_2(M^+)$ = 497, Found: $(M+H)^+$ = 498.0, $(M+NH_4)^+$ = 515.0.

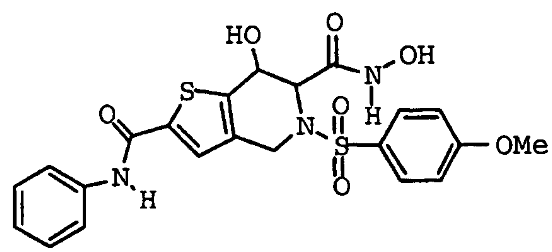
Example 24



Preparation of cis-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-2-(phenylmethoxycarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid

Utilizing benzyl alcohol, cis-7-hydroxy-5-(4-methoxy phenylsulfonyl)-2-(phenylmethoxycarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid was prepared from cis-2-iodo-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-6-(methoxycarbonyl)-4,5,6,7-tetrahydrothieno [3,2-c]pyridine in the same manner as cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(methoxycarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid: White solid; TLC, Rf = 0.20(EtOAc); ^{1}H NMR ($CDCl_3$) δ 3.90(s, 3H), 4.44(dd, 2H), 4.70(bs, 1H), 4.90(bs, 1H), 5.28(s, 2H), 5.30(bs, 1H), 6.98(d, 2H), 7.38(m, 5H), 7.80(d, 2H), 9.65(bs, 1H); MS: Caldc. $C_{23}H_{22}N_2O_8S_2(M^+)$ = 518, Found: $(M+H)^+$ = 519.1, $(M+NH_4)^+$ = 536.0.

Example 25

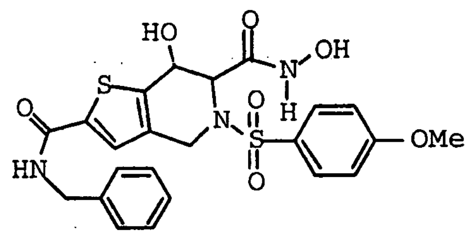


Preparation of cis-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-2-(N-phenylaminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid

Utilizing aniline, cis-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-2-(N-phenylaminocarbonyl)-4,5,6,7-tetrahydro thieno-[3,2-c]-pyridine-6-hydroxamic acid was prepared from cis-2-iodo-7-hydroxy-5-(4-methoxyphenylsulfonyl)-6-

(methoxycarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c] pyridine in the same manner as cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(4-morpholinocarbonyl)-4,5,6,7-tetrahydro thieno-[3,2-c]-pyridinyl-6-hydroxamic acid: White solid; TLC, Rf = 0.55(10% MeOH in CH_2Cl_2); ^1H NMR (acetone-d_6) δ 3.70(s, 3H), 4.40(dd, 2H), 4.70(s, 1H), 4.75(s, 1H), 5.00(bs, 1H), 6.90 - 7.70(series of m, 10H), 9.35(bd, 1H); MS: Caldc. $C_{22}H_{20}N_3O_7S_2$ (M^+) = 503, Found: $(M+H)^+$ = 504.0, $(M+NH_4)^+$ = 521.0.

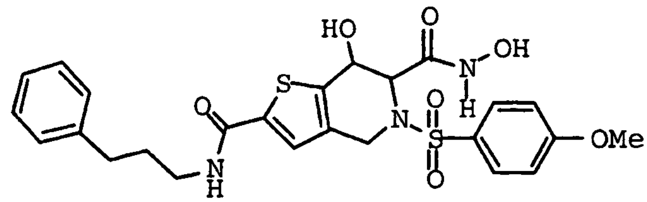
Example 26



Preparation of cis-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-2-(N-benzylaminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid

Utilizing benzylamine, cis-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-2-(N-benzylaminocarbonyl)-4,5,6,7-tetrahydro thieno-[3,2-c]-pyridine-6-hydroxamic acid was prepared from cis-2-iodo-7-hydroxy-5-(4-methoxyphenylsulfonyl)-6-(methoxycarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c] pyridine in the same manner as cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(4-morpholinocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid: White solid; TLC, Rf = 0.50(10% MeOH in CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 3.85(s, 3H), 4.42(dd, 2H), 4.50(bs, 1H), 4.72(bs, 1H), 4.88(bs, 1H), 6.30(bs, 1H), 6.90-7.90 (series of m, 10H); MS: Caldc. $C_{23}H_{23}N_3O_7S_2$ (M^+) = 517, Found: $(M+H)^+$ = 518.1, $(M+NH_4)^+$ = 535.2.

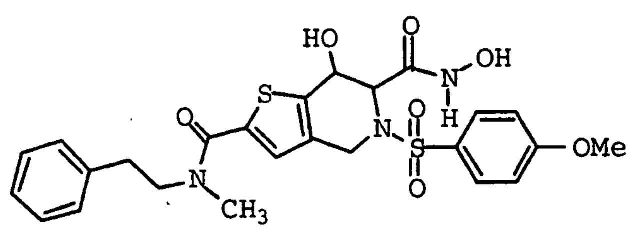
Example 27



Preparation of cis-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-2-(N-(3-phenylpropyl)aminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid

Utilizing 3-phenylpropylamine, cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-(3-phenylpropyl)amino carbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid was prepared from cis-2-iodo-7-hydroxy-5-(4-methoxyphenylsulfonyl)-6-(methoxycarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine in the same manner as cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(4-morpholinocarbonyl)-4,5,6,7-tetrahydro thieno-[3,2-c]-pyridinyl-6-hydroxamic acid: White solid; TLC, Rf = 0.60(10% MeOH in CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 1.80(m, 2H), 2.58(m, 2H), 3.30(m, 2H), 3.70(bs, 3H), 4.38(bm, 2H), 4.70(bs, 1H), 4.94(bs, 1H), 5.10(bs, 1H), 6.82(d, 2H), 7.00 - 7.20(series of m, 6H), 7.80(d, 2H), 9.90(bs, 1H); MS: Caldc. $C_{25}H_{27}N_3O_7S_2(M^+)$ = 545, Found: $(M+H)^+$ = 546.0, $(M+NH_4)^+$ = 563.0.

Example 28

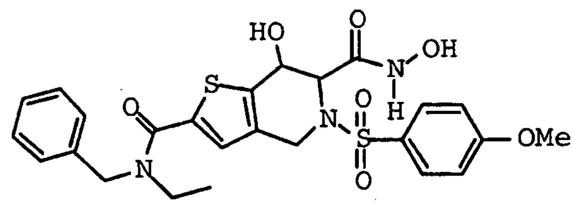


Preparation of cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-methyl-N-(phenethyl)aminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid

Utilizing N-methyl-N-(phenethyl)amine, cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-methyl-N-(phenethyl)amino

carbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid was prepared from cis-2-iodo-7-hydroxy-5-(4-methoxyphenylsulfonyl)-6-(methoxycarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine in the same manner as cis-7-hydroxy-2-(4-morpholinocarbonyl)-5-(4-methoxy phenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid: White solid; Rf = 0.20 (5% MeOH in EtOAc); ^{1}H NMR (acetone-d_6) δ 2.92(t, 2H), 3.12 (bs, 3H), 3.71(t, 2H), 3.88(s, 3H), 4.58(s, 2H), 4.90(s, 1H), 5.05(s, 1H), 7.00(d, 2H), 7.25(m, 6H), 7.80(d, 2H), 7.90(bs, 1H), 10.25(bs, 1H); MS: Calc. $C_{25}H_{27}N_3O_7S_2(M^+)$ = 545, Found: $(M+H)^+$ = 546.0, $(M+NH_4)^+$ = 563.1.

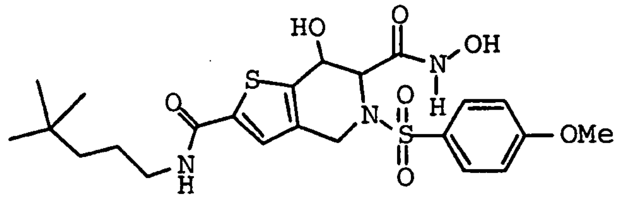
Example 29



Preparation of cis-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-2-(N-benzyl-N-ethylaminocarbonyl)-4,5,6,7-tetrahydro thieno-[3,2-c]-pyridine-6-hydroxamic acid

Utilizing N-ethylbenzylamine, cis-7-hydroxy-5-(4-methoxy phenylsulfonyl)-2-(N-benzyl-N-ethylaminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid was prepared from cis-2-iodo-7-hydroxy-5-(4-methoxyphenylsulfonyl)-6-(methoxycarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine in the same manner as cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(4-morpholinocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid: White solid; Rf = 0.15 (EtOAc); ^{1}H NMR (acetone-d_6) δ 1.20(bm, 3H), 3.50(m. 2H), 3.80(s, 3H), 4.50(bs, 1H), 4.70(bs, 1H), 4.85(bs, 1H), 5.00(bs, 1H), 6.90(d, 2H), 7.05(s, 1H), 7.30(m, 5H), 7.78(d, 2H), 10.20(bs, 1H);); MS: Calc. $C_{25}H_{27}N_3O_7S_2(M^+)$ = 545, Found: $(M+H)^+$ = 546.0, $(M+NH_4)^+$ = 563.3.

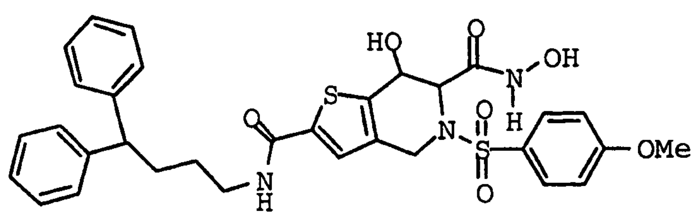
Example 30



Preparation of cis-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-2-(N-(4,4-dimethylpentyl)aminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid

Utilizing 4,4-dimethylpentylamine, cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-(4,4-dimethylpentyl)amino carbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid was prepared from cis-2-iodo-7-hydroxy-5-(4-methoxyphenylsulfonyl)-6-(methoxycarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine in the same manner as cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(4-morpholinocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid: White solid; TLC, Rf = 0.55 (10% MeOH in CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 0.90(s, 9H), 1.15(bm, 2H), 1.40(bm, 2H), 3.35(bm, 2H), 3.80(s, 3H), 4.32(bs, 2H), 4.80(bs, 1H), 4.85(bs, 1H), 5.15(bs, 1H), 6.90(d, 2H), 7.10(s, 1H), 7.78(d, 2H), 10.00(bs, 1H); MS: Caldc. $C_{22}H_{29}N_3O_7S_2$ (M^+) = 511, Found: $(M+H)^+$ = 512.2, $(M+NH_4)^+$ = 529.2.

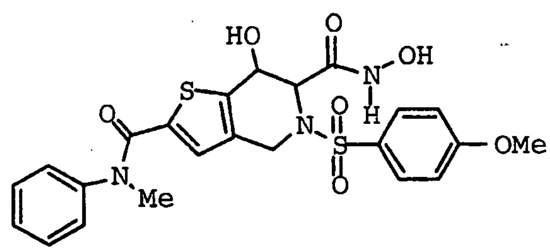
Example 31



Preparation of cis-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-2-(N-(4,4-diphenylbutyl)aminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid

Utilizing 4,4-diphenylbutylamine, cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-(4,4-diphenylbutyl)amino carbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid was prepared from cis-2-iodo-7-hydroxy-5-(4-methoxyphenylsulfonyl)-6-(methoxycarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine in the same manner as cis-7-hydroxy-5-(4-methoxyphenyl sulfonyl)-2-(4-morpholinocarbonyl)-4,5,6,7-tetrahydro thieno-[3,2-c]-pyridinyl-6-hydroxamic acid: White solid; Rf = 0.50 (10% MeOH in CH_2Cl_2); ^{1}H NMR (acetone-d_6) δ 1.50(m, 2H), 1.90(m, 2H), 3.35(bm, 2H), 3.70(bm, 1H), 3.92(s, 3H), 4.10(bs, 1H), 4.52(dd, 2H), 4.90(bs, 1H), 5.00(bs, 1H), 6.80-7.90(series of m, 15H); MS: Calc. $C_{31}H_{31}N_3O_7S_2$ (M^+) = 621, Found: $(M+H)^+$ = 622.3, $(M+NH_4)^+$ = 639.0, $(M-H)^-$ = 620.0.

Example 32

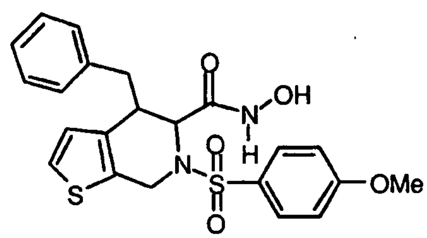


Preparation of cis- and trans-7-hydroxy-5-(4-methoxy phenylsulfonyl)-2-(N-phenyl-N-methylaminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid

Utilizing N-methylaniline, cis- and trans-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-phenyl-N-methylamino carbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid was prepared from 2-iodo-7-hydroxy-5-(4-methoxyphenylsulfonyl)-6-(methoxycarbonyl)-4,5,6,7-tetra hydrothieno[3,2-c]pyridine in the same manner as cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(4-morpholino carbonyl)-4,5,6,7-tetrahydro thieno-[3,2-c]-pyridinyl-6-hydroxamic acid. The diastereoisomers were separated to yield cis-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-

phenyl-N-methylaminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid: White solid; TLC, Rf = 0.55 (10% MeOH in EtOAc); ^{1}H NMR (acetone-d_6) δ 3.36(s, 3H), 3.85(s, 3H0, 4.30(s, 2H), 4.80(s, 1H), 4.90(s, 1H), 6.45(s, 1H), 7.00(d, 2H), 7.32(d, 2H), 7.40(m, 3H), 7.94(d, 2H), 10.25(s, 1H); MS: Calc. $C_{23}H_{23}N_3O_7S_2(M^+)$ = 517, Found: $(M+H)^+$ = 517.8, $(M+NH_4)^+$ =534.9; and trans-7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-phenyl-N-methyl aminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid: White solid; TLC, Rf = 0.55 (10% MeOH in EtOAc); ^{1}H NMR (acetone-d_6) δ 3.35(s, 3H0, 3.90(s, 3H0, 4.14(dd, 2H), 4.85(s, 1H), 4.90(s, 1H), 6.40(s, 1H), 7.02(d, 2H0, 7.31(d, 2H0, 7.42(m, 3H0, 7.78(d, 2H); MS: Caldc. $C_{23}H_{23}N_3O_7S_2(M^+)$ = 517, Found: $(M+H)^+$ = 517.9, $(M+NH_4)^+$ =534.9.

Example 33



Preparation of 4-trans-Benzyl-6-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydro-thieno[2,3,-c]pyridine-5-hydroxamic acid.

Step A: 3-Phenyl-2-thien-3-yl-acrylic acid

To a stirred solution of 3-thienylacetic acid (30 g, 211 mmol) in 200 mL acetic anhydride was added triethyl amine (29.4 mL, 211 mmol) and benzaldehyde (34.2 mL, 336 mmol). The reaction was heated to reflux for two hours under Argon with stirring. The reaction mixture was treated with 300 mL water and refluxed for 5 minutes, followed by cooling to room temperature and then submerging in an ice bath for 30 minutes. The solid precipitate was collected by filtration, washed with 600

mL of 50% aqueous acetic acid and 600 mL of water and dried overnight in a vacuum dessicator to afford 3-phenyl-2-thien-3-yl-acrylic acid as a pale tan solid and used directly in the next step: MS (M+H)+ 231, (M+NH4)+ 248. (Das et al., J. Med. Chem. 16(12):1361-1365, 1973)

Step B: 3-Phenyl-2-thien-3-yl-propionic acid

A suspension of 3-phenyl-2-thien-3-yl-acrylic acid (10.2 g, 44 mmol) in 200 mL of absolute ethanol in a Parr bottle was degassed by evacuation/purge with Argon before addition of Wilkinson's catalyst (1.07 g, 1.2 mmol). The reaction was hydrogenated in a Parr shaker apparatus with heating to 60-70°C under 50 psi of hydrogen for 20 hours. The solvent was removed by rotary evaporation, and the dark residue was dissolved in 400 mL of 1N sodium hydroxide and washed with 2 portions of 200 mL of ethyl acetate. The aqueous layer was acidified to pH 2 with 1N aqueous hydrochoric acid before extracting with 3 portions of 100 mL of ethyl acetate. The combined organic layers after acid treatment were dried with sodium sulfate, filtered, evaporated and dried in vacuo to afford 3-phenyl-2-thien-3-yl-propionic acid as a tan solid: MS (M-H)- 231

Step C: Methyl 3-Phenyl-2-thien-3-yl-propionate

To a solution of 3-phenyl-2-thien-3-yl-propionic acid (9 g, 38.7 mmol) in anhydrous methanol was slowly added thionyl chloride (1 mL, 13.7 mmol). The reaction was heated to reflux overnight, followed by removal of solvent under reduced pressure. The dark residue was diluted with ethyl acetate, washed with saturated aq sodium bicarbonate and brine. The organic phase was dried (sodium sulfate), filtered and evaporated to afford the methyl ester homogenous by TLC: MS (M+H)+ 247, (M+NH4)+ 264

Step D: 3-Phenyl-2-thiophen-3-yl-propionaldehyde

To a stirred cooled (-78°C) solution of methyl 3-phenyl-2-thien-3-yl-propionate (8.3 g,33.73 mmol) in 65 mL anhydrous toluene under Argon was added a pre-cooled (-78°C) solution of diisobutylaluminum hydride (52.5 mL of a 1 M solution in toluene, 52.5 mmol) dropwise, via cannula, so the internal temperature of the reaction does not rise above -65°C. After 25 minutes at -78°C, TLC indicated complete consumption of methyl ester, and the reaction was quenched by careful addition of precooled (-78°C) anhydrous methanol (32.6 mL) dropwise via cannula, so the internal temperature again does not rise above -65°C. After warming to ambient temperature overnight, the reaction was quenched by adding aqueous citric acid and extracted with ethyl acetate. The organic layer was washed with water, saturated aqueous sodium potassium tartrate, dried, filtered and evaporated to yield a crude product. The product was purified by silica gel flash chromatography using step gradient of hexanes/ethyl acetate 9:1; 8:1; 7:1; 3:1 to afford the aldehyde: MS (M+MeOH+NH4)+ 266

Step E: 2-Hydroxy-4-phenyl-3-thien-3-yl-butyronitrile

To a cooled 0°C solution of potassium cyanide (1.95 g, 29.9 mmol) in 1.8 mL water was added ammonium chloride (1.79 g, 33.5 mmol), concentrated ammonium hydroxide (20 mL, 143.79 mmol), and a solution of 3-phenyl-2-thiophen-3-yl-propionaldehyde (6.19 g, 29.44 mmol) in 60 mL of diethyl ether. The mixture was capped tightly before removing the ice bath and was stirred at room temperature overnight. The reaction was extracted with 4 portions of 50 mL of diethyl ether and 2 portions of 10 mL of ethyl acetate. The combined organic layers were dried (magnesium sulfate), filtered and evaporated to afford crude 2-hydroxy-4-phenyl-3-thien-3-yl-butyronitrile: MS $(M+H)^+$ 243.

Step F: 2-Hydroxy-4-phenyl-3-thien-3-yl-butyric acid

A suspension of 2-hydroxy-4-phenyl-3-thien-3-yl-butyronitrile (7.74 g, 29.44 mmol) in 75 mL concentrated hydrochloric acid was heated to reflux for 2 hours. The mixture was cooled to room temperature, and treated with concentrated aq potassium hydroxide to pH 5-6. The reaction was extracted with several portions of ethyl acetate, the organic layers were dried, filtered and evaporated to yield crude 2-hydroxy-4-phenyl-3-thien-3-yl-butyric acid: MS $(M-H)^-$ 261

Step G: Methyl 2-hydroxy-4-phenyl-3-thien-3-yl-butyrate

To a stirred solution of 2-hydroxy-4-phenyl-3-thien-3-yl-butyric acid (4.2 g, 16 mmol) in 80 mL of methanol was added 2.5 mL of concentrated sulfuric acid, and the mixture was refluxed for two hours. The solvent was removed *in vacuo*, and the residue was dissolved in ethyl acetate and washed with saturated sodium bicarbonate, and water. The combined organic phases were dried (magnesium sulfate), filtered and evaporated to afford crude product. This was purified by flash chromatography on silica gel using gradient elution of hexanes/ethyl acetate 9:1 to 8:1 to afford (a) pure faster eluting diastereomer as a clear oil, (b) a mixture of diastereomers and (c) slower eluting diastereomer as pale yellow oil: MS (M+H)+ 277, (M+NH4)+ 294

Step H: Methyl 2-(4-methoxyphenylsulfonyl)amino-4-phenyl-3-thien-3-yl-butyrate

To a cooled (0°C) solution of triphenylphosphine (2.91 g, 11 mmol) in 10 mL of anhydrous tetrahydrofuran was added diisopropyl azodicarboxylate (2.2 mL, 11.2 mmol) dropwise with stirring under Argon. After the white solid complex precipitated, a solution of methyl 2-hydroxy-4-phenyl-3-thien-3-yl-butyrate (1.38 g, 5 mmol, faster eluting diastereomer) in 12 mL of tetrahydrofuran is added dropwise via cannula, followed by a solution of

N-(tert-butoxycarbonyl)-p-methoxybenzenesulfonamide (3.06 g, 10.6 mmol) in 20 mL THF. The yellow-orange reaction was warmed to ambient temperature and heated to 35°C for four days under an atmosphere of Argon until all the hydroxy ester was consumed (TLC monitored). The solvent was removed *in vacuo* and the off-white foam was purified by flash chromatography on silica gel using a gradient of 0-3% ethyl acetate in 1:1 dichloromethane/ hexanes to afford pure methyl 2-(N-(tert-butoxy carbonyl)-N-(4-methoxyphenyl sulfonyl)amino)-4-phenyl-3-thien-3-yl-butyrate as a white foam of a single diastereomer: MS (M+H)+ 546, (M+NH4)+ 563

To a solution of methyl 2-(N-(tert-butoxycarbonyl)-N-(4-methoxyphenylsulfonyl)amino)-4-phenyl-3-thien-3-yl-butyrate (910 mg, 1.65 mmol, single diastereomer) in 27.3 mL CH_2Cl_2 was added trifluoroacetic acid (13.6 mL). The reaction was stirred for two hours at room temperature before removing all volatiles and azeotroping the residue with 2 by 20 mL portions of toluene *in vacuo* to afford crude methyl 2-(4-methoxy phenylsulfonyl)amino-4-phenyl-3-thien-3-yl-butyrate as a single diastereomer: MS (M+H)+ 446, (M+NH4)+ 463

<u>Step I: Methyl 4-(N-carboxymethyl-N-(4-methoxyphenyl sulfonyl)-amino)-4-phenyl-3-thien-3-yl-butyrate</u>
To a cooled (0°C) solution of the crude methyl 2-(4-methoxyphenylsulfonyl)amino-4-phenyl-3-thien-3-yl-butyrate (single diastereomer) in 60 mL of tetrahydrofuran:N,N-dimethylformamide (2:1) was added a solution of potassium bis-(trimethylsilyl)amide in toluene (4.64 mL of a 0.5 M solution, 2.32 mmol) dropwise with stirring under Argon. The solution was stirred at 0°C for 15 minutes before addition of tert-butyl bromoacetate (0.342 mL, 2.32 mmol). The reaction was stirred overnight at ambient temperature, then worked up by dilution with ethyl acetate and aqueous 2 M

ammonium chloride. The organic phase was washed with saturated aqueous sodium bicarbonate, dried, filtered and evaporated to afford crude methyl 2-(N-(tert-butoxycarbonylmethyl)-N-(4-methoxyphenylsulfonyl)-amino)-4-phenyl-3-thiophen-3-yl-butyrate as a mixture of two diastereomers: MS (M+H)+ 560, (M+NH4)+ 577.

To a cooled (0°C) solution of the crude methyl 2-(N-(tert-butoxycarbonylmethyl)-N-(4-methoxyphenylsulfonyl)-amino)-4-phenyl-3-thiophen-3-yl-butyrate in 50 mL CH_2Cl_2 was added 15 mL of trifluoroacetic acid. The reaction was stirred at 0°C for 3 hours before removing all volatiles and co-evaporation with 2 portions of 20 mL of toluene. The crude product was purified by flash chromatography on silica gel using a gradient of 0-7% MeOH in CH_2Cl_2 to afford methyl 4-(N-carboxymethyl-N-(4-methoxyphenylsulfonyl)-amino)-4-phenyl-3-thien-3-yl-butyrate as a mixture of the two diastereomers: MS (M+H)+ 504, (M+NH4)+ 521

Step J: Methyl 4-benzyl-6-(4-methoxyphenylsulfonyl)-8-oxo-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-carboxylate; and Methyl 4-benzyl-6-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrothieno[2,3,-c]pyridine-5-carboxylate

To a stirred solution of methyl 4-(N-carboxymethyl-N-(4-methoxyphenylsulfonyl)-amino)-4-phenyl-3-thien-3-yl-butyrate (476 mg, 0.946 mmol) in 7.7 mL anhydrous dichloromethane containing 22 µL of N,N-dimethylformamide was added oxalyl chloride (180 µL, 2 mmol) dropwise under Argon. The clear yellow solution turned turbid with evolution of gas. The reaction was stirred for 2 hours at room temperature before cooling to -78°C in an acetone/CO2(s) bath. To the reaction was added tin tetrachloride (151 µL, 1.29 mmol) dropwise. The reaction turned brownish, and was allowed to warm slowly overnight with stirring under Argon. To the dark-blue

reaction mixture was added 1N hydrochloric acid and dichloromethane, and the aqueous layer was extracted repeatedly with dichloromethane and ethyl acetate. The combined organic layers were dried (sodium sulfate), filtered and evaporated to afford a crude product. This was purified by flash chromatography on silica gel to afford the 6-membered ring product methyl 4-benzyl-6-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[2.3.-c] pyridine-5-carboxylate as a mixture of diastereomers (MS M+H 458, M+NH4 475) and the 7-membered ring product methyl 4-benzyl-6-(4-methoxyphenylsulfonyl)-8-oxo-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-carboxylate as a mixture of diastereomers (MS (M+H)+ 486, (M+NH4)+ 503).

Step K: 4-Benzyl-6-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[2.3.-*c*]pyridine-5-hydroxamic acid

To a stirred solution of methyl 4-benzyl-6-(4-methoxy phenylsulfonyl)-4,5,6,7-tetrahydrothieno[2.3.-c] pyridine-5-carboxylate (16.6 mg, 0.036 mmol) in 2 mL of methanol was added 1 mL of 1N NaOH. The reaction was stirred overnight at room temperature before removing the methanol under reduced pressure. The aqueous solution was acidified with 1N aqueous hydrochloric acid, and extracted three times with ethyl acetate. The combined organic layers were dried (sodium sulfate), filtered, evaporated and dried by co-evaporation with anhydrous toluene (twice) to afford crude 4-benzyl-6-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[2.3.-c] pyridine-5-carboxylic acid: MS (M-H)- 442

To a 0°C solution of 4-benzyl-6-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydrothieno[2.3.-c]pyridine-5-carboxylic acid (14 mg, 0.0316 mmol) in 1.5 mL of dichloromethane was added hydroxylamine hydrochloride (13.5 mg, 0.194 mmol), PyBroP (Bromo-tris-pyrrolidino-phosphonium hexafluoro-phosphate, 45 mg, 0.0965 mmol)

and N,N-diisopropylethylamine (35 µL, 0.201 mmol) with stirring under Argon. The reaction was warmed slowly to room temperature overnight. To the reaction was added 1N hydrochloric acid, and the aqueous was extracted with ethyl acetate. The crude product was purified by flash chromatography on silica gel using hexanes-ethyl acetate-acetic acid (5:5:0.1) to afford pure 4-trans-benzyl-6-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro thieno[2.3.-c]pyridine-5-hydroxamic acid which was characterized by NMR analysis to have trans stereochemistry: (M+H)+ 459, (M+NH4)+ 476

Example 34

Alternative Preparation of Methyl 2-(4-methoxyphenyl sulfonyl)amino-4-phenyl-3-thien-3-yl-butyrate

Step A: N-(3-Phenyl-2-thien-3-yl-propylidene)-4-methoxyphenylsulfonamide

To a solution of 15.0 g 3-phenyl-2-thien-3-yl-propion aldehyde (69.4 mmol) in 300 mL of anhydrous toluene was added 12.3 g of freshly activated powdered 5 Å sieves, 400 mg of Amberlyst 15 resin and 18.2 g (97.2 mmol, 1.4 eq) of p-methoxyphenylsulfonamide. The reaction was refluxed with a Dean-stark trap under Argon atmosphere for two days. The reaction was filtered through a pad of Celite and the filtrate was evaporated to dryness to afford N-(3-phenyl-2-thien-3-yl-propylidene)-4-methoxy phenylsulfonamide: MS $(M+H)^+$ 386, $(M+NH4)^+$ 403

Step B: N-(1-Cyano-3-phenyl-2-thien-3-ylpropyl)-4-methoxyphenylsulfonamide

To a stirred solution of N-(3-phenyl-2-thien-3-yl-propylidene)-4-methoxybenzenesulfonamide (16.6 g, 43.0 mmol) in 200 mL of N,N-dimethylformamide was added potassium cyanide (18g, 289.7 mmol). The reaction was stirred overnight at ambient temperature, followed by

heating to 75°C for two days. The reaction was diluted with ethyl acetate, washed with 4 portions of 500 mL of water, and the crude residue after filtration and evaporation was purified by flash chromatography on silica gel to afford N-(1-cyano-3-phenyl-2-thien-3-ylpropyl)-4-methoxyphenylulfonamide as a mixture of diastereomers: MS (M+H)+ 413, (M+NH4)+ 430

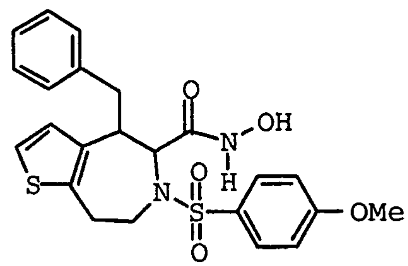
Step C: 2-(4-Methoxyphenylsulfonylamino)-4-phenyl-3-thien-3-yl-butyric acid

To a solution of 14.03 g of N-(1-cyano-3-phenyl-2-thien-3-ylpropyl)-4-methoxyphenylsulfonamide (34.04 mmol) in 600 mL of dioxane was added 1.2 L of concentrated hydrochloric acid. The reaction was heated to reflux overnight, and after cooling, 150 mL of 10 N aq sodium hydroxide was added to the reaction. The reaction mixture was extracted with ethyl acetate and several times with dichloromethane. The combined organic phases were dried, filtered and evaporated to afford the crude 2-(4-methoxyphenylsulfonylamino)-4-phenyl-3-thien-3-yl-butyric acid as a mixture of diastereomers: MS (M+H)+ 432, (M+NH4)+ 449

Step D: Methyl 2-(4-methoxyphenylsulfonyl)amino-4-phenyl-3-thien-3-yl-butyrate

To a solution of the crude 2-(4-methoxyphenylsulfonyl amino)-4-phenyl-3-thien-3-yl-butyric acid in 300 mL of anhydrous methanol was added dropwise 1.5 mL of thionyl chloride. The reaction was refluxed overnight with stirring. The solvents were removed by rotary evaporation, aqueous workup followed by azeotroping with toluene afforded crude methyl 2-(4-methoxyphenyl sulfonyl)amino-4-phenyl-3-thien-3-yl-butyrate as a mixture of diastereomers: MS (M+H)+ 446, (M+NH4)+ 463

Example 35



Preparation of (+/-)-4-trans-Benzyl-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid

Step A: Methyl 4-Benzyl-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate

To a stirred solution of methyl 4-benzyl-6-(4-methoxyphenylsulfonyl)-8-oxo-5,6,7,8-tetrahydro-4H-thieno [2,3,d]azepine-5-carboxylate (52.9 mg, 0.11 mmol) in 3 mL of dichloromethane was added 1.08 mL of trifluoroacetic acid, followed by 375 µL of triethylsilane. The reaction was stirred for two days before removing all volatiles *in vacuo*. The residue was dried by co-evaporation with 2 portions of 10 mL of toluene and purified by flash chromatography on silica gel to afford methyl 4-benzyl-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate: MS (M+H)+ 472, (M+NH4)+ 489

Step B: 4-Benzyl-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylic acid

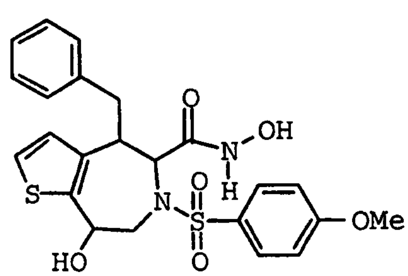
To a solution of methyl 4-benzyl-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate (24.8 mg, 0.053 mmol) in 2 mL of methanol was added 2 mL of 1 N NaOH. The solution was stirred overnight before removing all solvents *in vacuo*. The aqueous solution was acidified with 1N hydrochloric acid and extracted with ethyl acetate. The organic phases were dried, filtered and evaporated to afford crude 4-benzyl-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-

4H-thieno[2,3-d]azepine-5-carboxylic acid: MS (M-H)- 456

Step C: 4-Benzyl-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid

To a solution of 4-benzyl-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylic acid (22.4 mg, 0.049 mmol) in 2.4 mL of anhydrous dichloromethane cooled to 0°C was added hydroxylamine hydrochloride (26 mg, 0.37 mmol), PyBrOP (Bromo-tris-pyrrolidino-phosphonium hexafluorophosphate, 82 mg, 0.175 mmol), and N,N-diisopropylethylamine (75 µL, 0.43 mmol). The reaction was stirred overnight at room temperature before adding 1 N hydrochloric acid and extracting with dichloromethane and ethyl acetate. The combined organic phases were dried (sodium sulfate), filtered and evaporated. The crude product was purified by flash chromatography using hexanes-ethyl acetate-acetic acid (5:5:0.1) to afford 11.0 mg of pure (+/-)-4-trans-benzyl-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid: MS (M+H)+ 473, (M+NH4)+ 490

Example 36



Preparation of (+/-)-4-Benzyl-8-cis-hydroxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid

Step A: 4-Benzyl-9-(4-methoxyphenylsulfonyl)-11-oxa-3-thia-9-aza-tricyclo[6.2.2.0^{0,0}]dodeca-2(6),4-dien-12-one

To a cooled (0°C) suspension of methyl 4-benzyl-6-(4-methoxyphenylsulfonyl)-8-oxo-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-carboxylate, as a mixture of two diastereomers, (83.6 mg, 0.17 mmol) in 8 mL of anhydrous methanol was added sodium borohydride (3.6 mg, 0.095 mmol). The reaction was stirred for one hour at 0°C before evaporating the methanol under reduced pressure. The reaction was then partitioned between water and ethyl acetate, and the crude product after evaporation of the organic phases was purified by flash chromatography to afford a diastereomeric mixture of hydroxy methyl esters and the lactone 4-benzyl-9-(4-methoxyphenylsulfonyl)-11-oxa-3-thia-9-aza-tricyclo [6.2.2.0^{0,0}]dodeca-2(6),4-dien-12-one: (M+H)+ 456, $(M+NH_4)_+$ 473

Step B: (+/-) 4-Benzyl-8-cis-hydroxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid

To a solution of sodium methoxide (16 mg, 0.29 mmol) in 0.7 mL anhydrous methanol was added hydroxylamine hydrochloride (20 mg, 0.28 mmol). After 2 hours stirring at ambient temperature, the solid precipitate was removed by filtration and the resulting solution was added to 7-benzyl-9-(4-methoxyphenylsulfonyl)-11-oxa-3-thia-9-aza-tricyclo[6.2.2.0^{0,0}]dodeca-2(6),4-dien-12-one (6.3 mg, 0.013 mmol). The solution was stirred overnight before removing all solvents. The residue was diluted with ethyl acetate, washed with 1N HCl, dried (sodium sulfate), filtered and evaporated. The crude product was purified by flash chromatography to afford 4-benzyl-8-hydroxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid as a single diastereomer: MS $(M+H)^+$ 489, $(M+NH_4)^+$ 506

Example 37

Preparation of: 4-cis-Benzyl-8-cis-hydroxy-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid (the other diastereomer)

Step A: Methyl 4-benzyl-8-hydroxy-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-carboxylate

A solution of methyl 4-benzyl-6-(4-methoxyphenyl sulfonyl)-8-oxo-5,6,7,8-tetrahydro-4H-thieno[2,3,-d]azepine-5-carboxylate (the faster eluting diastereomer, 330 mg, 0.68 mmol) in 68 mL of anhydrous tetrahydrofuran was cooled to -78°C before addition of L-Selectride (0.7 mL of a 1 M solution in tetrahydrofuran, 0.7 mmol). After 20 minutes stirring under Argon at -78°C, the reaction was quenched with saturated aqueous ammonium chloride, then allowed to warm to room temperature. The reaction was extracted twice with ethyl acetate and the combined organic layers were dried over sodium sulfate, filtered, evaporated and purified by flash chromatography on silica gel (gradient of 0-10% ethyl acetate in 1:1 dichloromethane/hexanes) to afford a faster eluting diastereomer (used immediately in next step) and slower eluting diastereomer of methyl 4-benzyl-8-hydroxy-6-(4-methoxy phenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d] azepine-5-carboxylate: $(M-H)^-$ 486.

Step B-1: 4-benzyl-8-(tert-butyldimethylsilyloxy)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-carboxylic acid (From Step A Faster Diastereomer)

To a solution of the faster eluting diastereomer of methyl 4-benzyl-8-hydroxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-carboxylate

(205 mg, 0.42 mmol) in 30 mL of methanol was added 18 mL of 1N aqueous sodium hydroxide. The reaction was stirred at room temperature overnight before evaporating the methanol. The aqueous solution was acidified to pH 4 with 1N hydrochloric acid and extracted with ethyl acetate several times. The combined organic layers were dried (sodium sulfate), filtered and evaporated to yield 4-benzyl-8-hydroxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-carboxylic acid as a purple oil and dried by co-evaporation with toluene: (M-H)- 472.

To a suspension of 4-benzyl-8-hydroxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-carboxylic acid (0.42 mmol) in 20 mL of anhydrous dichloromethane was added N,N-diisopropylethylamine (0.63 mL, 0.62 mmol) and tert-butyldimethylsilyl trifluoromethanesulfonate (0.557 mL, 0.42 mmol). The solution was stirred overnight at room temperature before adding saturated aqueous ammonium chloride. The aqueous layer was extracted with dichloromethane and ethyl acetate, and the combined organic layers were dried (sodium sulfate), filtered and concentrated to an oil. The oil was dissolved in 2.5 mL of methanol and stirred with 290 mg (2 mmol) of anhydrous potassium carbonate for 2 hours at ambient temperature. The methanol was evaporated, aqueous ammonium chloride and 300 µL of glacial acetic acid were added (pH~5), and extracted with several portions of ethyl acetate. The combined organic layers were dried, filtered, concentrated and chromatographed on silica gel (2-mm Chromatotron plate using a gradient of 20 to 40% ethyl acetate - 1% acetic acid in hexanes) to yield a faster eluting diastereomer and a slower eluting diastereomer of 4-benzyl-8-(tert-butyldimethylsilyloxy)-6-(4-methoxy phenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d] azepine-5-carboxylic acid: (M-H)- 586, (M+NH4)+ 605.

Step B-2: 4-benzyl-8-(tert-butyldimethylsilyloxy)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-carboxylic acid (From Step A Slower Diastereomer)

Analogous procedures were carried out with the slower eluting diastereomer of methyl 4-benzyl-8-hydroxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno [2,3,d]azepine-5-carboxylate to yield a single diastereomer of 4-benzyl-8-(tert-butyldimethylsilyloxy)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-carboxylic acid having an identical NMR and TLC mobility to the faster eluting diastereomer of Step B-1.

Step C-1: 4-cis-benzyl-8-cis-(tert-butyldimethyl silyloxy)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid (From Step B Faster Diastereomer)

4-Benzyl-8-(tert-butyldimethylsilyloxy)-6-(4-methoxy phenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d] azepine-5-carboxylic acid (the faster eluting diastereomer, 48 mg, 0.08 mmol) was dried by co-evaporation with anhydrous toluene and dissolved in 4 mL of anhydrous N,N-dimethylformamide containing O-tert-butyldimethylsilyl hydroxylamine (77 mg, 0.52 mmol). The solution was cooled to -20°C in an ice/methanol bath. N,N-Diisopropylethylamine (0.075 mL, 0.37 mmol) was added, followed by HATU (*O*-7-(7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate, 151 mg, 0.39 mmol). The yellow reaction solution was warmed slowly and stirred overnight under Argon. The reaction was quenched with saturated ammonium chloride containing 100 µL of acetic acid (pH ~4), and extracted twice with ethyl acetate. The combined organic layers were dried (sodium sulfate), filtered, concentrated and purified by chromatography on silica gel (1-mm Chromatotron plate,

gradient of 0 to 3 % methanol in dichloromethane) to afford 4-cis-benzyl-8-cis-(tert-butyldimethyl silyloxy)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid.

Step C-2: 4-trans-benzyl-8-(tert-butyldimethyl silyloxy)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid (From Step B Slower Diastereomer)

Analogous procedures were carried out with the slower eluting diastereomer of 4-benzyl-8-(tert-butyldimethyl silyloxy)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-carboxylic acid to yield 4-trans-benzyl-8-(tert-butyldimethyl silyloxy)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid.

Step D-1: 4-cis-benzyl-8-cis-(hydroxy)-6-(4-methoxy phenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d] azepine-5-hydroxamic acid (From Faster Diastereomer of Step C)

To a solution of tetrabutylammonium fluoride in tetrahydrofuran (0.5mL of a 1M solution) was added 15 µL of glacial acetic acid. To a cooled (0°C) solution of 4-cis-benzyl-8-cis-(tert-butyldimethylsilyloxy)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno [2,3,d]azepine-5-hydroxamic acid (faster eluting diastereomer, 35.9 mg, 0.06 mmol) in 8.6 mL of anhydrous THF was added the tetrabutyl ammonium fluoride solution buffered with acetic acid (0.16 mL, 0.16 mmol). The reaction was allowed to stir and warm to ambient temperature for five hours before diluting with ethyl acetate and washing with saturated ammonium chloride. The organic layer was dried (sodium sulfate), filtered, evaporated and purified by silica gel chromatography (1-mm Chromatotron plate, gradient of 0 to 6% methanol in dichloromethane) to afford 4-cis-benzyl-8-cis-(hydroxy)-

6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno [2,3,d]azepine-5-hydroxamic acid: (M-H)- 487, (M+NH4)+ 506

Step D-2: 4-trans-benzyl-8-(hydroxy)-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid (From Slower Diastereomer of Step C)
Analogous procedures were carried out with the slower eluting diastereomer of 4-trans-benzyl-8-(tert-butyl dimethylsilyloxy)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid to yield 4-trans-benzyl-8-(tert-butyldimethyl silyloxy)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid.

Example 38

Preparation of Methyl 3-(4-Benzyl-thien-3-yl)-2-(tert-butoxycarbonylamino)propionate

Step A: 4-Benzyl-thiophene-3-carboxaldeyde
3-Benzyl-4-bromo-thiophene (12.7g, 50.1 mmol) is dissolved in 100 ml dry diethylether and cooled to -70°C. Butyllithium (22.0 ml, 2.5 M in Hexane) is added drop-wise at -70°C and the reaction is stirred for 5 minutes. Dimethylformamide (DMF) is added in one shot and the reaction mixture is stirred for 15 min. and then allowed to warm to 0°C. The reaction mixture is quenched with water and neutralized. The organic phase is separated and the water phase is extracted twice with diethylether. The combined organic extracts are dried with $MgSO_4$, filtered and the solvent is evaporated. Flash-chromatography, hexane/ethylacetate; 5:1 afforded the product: Cal. 203.3, found $(MH)^+$ 203. (MacDowell and Wisowaty, J. Org. Chem. 1971, 36(26), 3999-4004)

Step B: Methyl 3-(4-benzyl-thien-3-yl)-2-(tert-butoxycarbonyl amino)acrylate

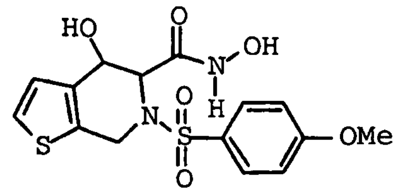
Under an Argon blanket, sodium hydride (493 mg, 12.3 mmol) is suspended in dry hexane (20 ml) and dry tetrahydrofuran (THF). The suspension is cooled to 0°C. Methyl tert-butoxycarbonylamino-(dimethoxyphosphoryl) acetate (3.33 g, 11.2 mmol) is dissolved in dry THF (20 ml) and added drop-wise to the reaction suspension. 4-Benzyl-thiophene-3-carboxaldeyde (3.69 g, 11.2 mmol) is dissolved in 20 ml THF and added drop-wise to the reaction. The reaction is allowed to warm to room temperature and is stirred for 3 h. After an aqueous work-up, the product is isolated from the organic phase by flash-chromatography (Hexane/Ethylacetate; 6:1): Cal. 374.5, found $(MH)^+$ 374.

Step C: Methyl 3-(4-Benzyl-thien-3-yl)-2-(tert-butoxycarbonylamino)propionate

Methyl 3-(4-benzyl-thien-3-yl)-2-(tert-butoxycarbonyl amino)acrylate (3.43 g, 9.2 mmol) is dissolved in 30 ml benzene/ethanol 4:1. The reaction solution is hydrogenated under shaking at 50°C at 60 psi using Chlorotris(triphenylphosphine)rhodium(I) (Wilkinson's catalyst). Initially, 25% (160 mg. 0.17 mmol) of the total amount (640 mg, 0.69 mmol) of the Wilkinson's catalyst is added and thereafter every 8-10 hours another 25% of the catalyst is added. The reaction is complete after 48 hours. The solvent is evaporated and the obtained dark oil is purified by flash-chromatography, Hexane/Ethylacetate (gradient 5-18%): Cal. 376.5, found $(MH)^+$ 376.2.

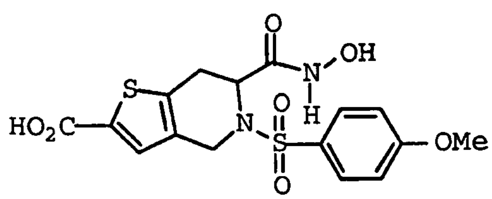
Example 39

4-Hydroxy-6-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-5-hydroxamic acid



Under an Argon atmosphere, 4-hydroxy-6-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-5-carboxylic acid (70 mg, 0.19 mmol) is dissolved in 3 ml dimethylformamide (DMF) and cooled to -30°C. O-(tert-Butyldimethylsilyl)hydroxylamine (36 mg, 0.24 mmol) and Hûnigs Base (50 µl, 0.24 mmol) are added and then O-(7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HATU) (79 mg, 0.21 mmol) is added. The reaction mixture is stirred for 15 min. and then allowed to warm to room temp. (about 1h). The solvent is evaporated at high vacuum and the obtained oil is purified by flash-chromatography ($CHCl_3$/MeOH; 9:1, followed by $CHCl_3$/MeOH, 9:1, cont. 1% Acetic Acid): Cal. 385.5, found $(MH)^+$ 385.2.

<u>Example 40</u>



<u>Preparation of 2-carboxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-6-hydroxamic acid</u>

<u>Step A: 2-Iodo-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-carboxylic acid</u>

5-(4-Methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-carboxylic acid (1.19 g, 3.4 mmol) is dissolved in 60 ml dry Tetrahydrofuran (THF) and cooled to -78°C. A solution of lithium diisopropylamide (3.55 ml, 7.1 mmol) in 5 ml THF is added drop-wise to the reaction mixture. The reaction

is stirred for 20 min. Iodine (0.86 g, 3.4 mmol) in 20 ml THF is added drop-wise to the reaction solution. The reaction is allowed to warm to room temp. (~1h) and is quenched with sat. NH_4Cl-solution. The organic phase is separated and the water phase is extracted twice with ethylacetate (50 ml). The water phase is acidified and extracted one more time with ethylacetate. The combined organic extracts are washed with sodium thiosulfate solution, dried with $MgSO_4$, filtrated and the solvent is evaporated in vacuo affording 2-iodo-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-carboxylic acid as a yellow foam: ^{1}H NMR (DMSO) δ 7.78 (d, 2H), 7.10(m, 3H), 5.0(d, 1H), 4.55(d, 1H), 4.3(d, 1H), 3.81(s, 3H), 3.2(m, 1H), 2.9(dd, 1H).

<u>Step B: 2-Iodo-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-carboxylic acid benzhydryloxy-amide</u>

To 2-iodo-5-(4-Methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-carboxylic acid (1.62 g, 3.37 mmol) in 25 ml dry Dimethylformamide (DMF) is added O-benzhydryl-hydroxylamine (0.95 g, 4.05 mmol), 1-hydroxyybenzotriazole (HOBt) (0.52 g, 3.37 mmol) and 1-(3-dimethylaminopropyl)-3-ethyl-carbodiimide hydrogen chloride (EDC) (0.78 g, 4.05 mmol). The reaction mixture is stirred for 4 h at room temp. The reaction mixture is concentrated in vacuo and the residue is purified by flash chromatography (Hexane/Ethyl acetate; 3:2) affording 2-iodo-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-carboxylic acid benzhydryloxy-amide: ^{1}H NMR (DMSO) δ 11.25(s, 1H), 7.68(d, 2H), 7.3(m, 10H), 7.08(m, 3H), 5.75(s, 1H), 4.75 (d, 1H), 4.55(d, 1H), 4.35(d, 1H), 3.85(s, 3H), 2.75 (m, 2H).

Step C: 2-(methoxycarbonyl)-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-6-carboxylic acid benzhydryloxy-amide

To 2-iodo-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-carboxylic acid benzhydryloxy-amide (140 mg, 0.21 mmol) in 10 ml tetrahydrofuran/ methanol (1:1) is added triethylamine (33 µl, 0.23 mmol) and the reaction solution is deoxygenated and saturated with Argon. Tetrakis (triphenylphosphine)palladium (0) (30 mg, 0.02 mmol) is added and the reaction solution is saturated with carbon monoxide (CO). The reaction is refluxed over night at 70°C. Evaporation of the solvents and flash-chromatography (Hexane/Ethylacetate; 3:2) afforded 2-(methoxycarbonyl)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-6-carboxylic acid benzhydryloxy-amide: Cal 593.7, found 592.8.

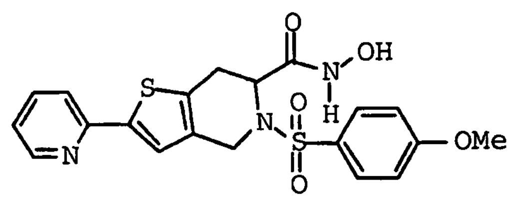
Step D: 2-(methoxycarbonyl)-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-6-hydroxamic acid

To 2-(methoxycarbonyl)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-6-carboxylic acid benzhydryloxy-amide (53 mg, 0.09 mmol) in dichloromethane/trifluoroacetic acid (3:1, 4 ml) is added triethylsilane (14.3 µl, 0.09 mmol) and the reaction mixture is stirred for 1 h. The solvents are evaporated and the residue is dissolved in DCM and mixed with diethylether and hexane. A white precipitate occurs which is filtered giving 2-(methoxycarbonyl)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-6-hydroxamic acid as a white powder: Cal. 427.5, found $(MH)^+$ 427.

Step E: 2-carboxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-6-hydroxamic acid

2-(Methoxycarbonyl)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-6-hydroxamic acid (20 mg, 0.047 mmol) in 4 ml tetrahydrofuran/water (1:1) is stirred at room temp. for 1.5 h. The reaction mixture is acidified with 2N HCl to pH 3. The organic phase is separated and the water phase is extracted twice with ethyl acetate. The solvents are evaporated and the remaining solid is lyophilized to yield 2-carboxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[2,3-c] pyridine-6-hydroxamic acid: Cal. 412.5, found $(MH)^+$ 413.0.

Example 41



Prpearation of 5-(4-methoxyphenylsulfonyl)-2-pyrid-2-yl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-hydroxamic acid

Step A: 5-(4-methoxyphenylsulfonyl)-2-pyrid-2-yl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-carboxylic acid benzhydryloxy-amide

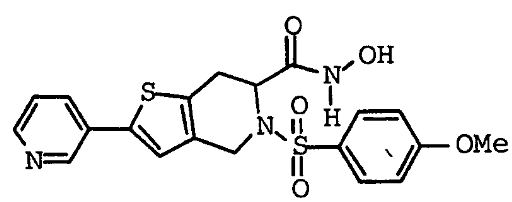
Under an Argon atmosphere, 2-(tributylstannyl)pyridine (920 mg, 2.5 mmol) in 10 ml Tetrahydrofuran (THF) is cooled to -78°C. Butyllithium (1 ml, 2.5M) is added drop-wise and the reaction mixture is stirred for 10 minutes. A ZnCl solution (5 ml, 0.5 M, 2.5 mmol) is added. The reaction is allowed to warm room temp. and added via syringe to 2-iodo-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-carboxylic acid benzhydryloxy-amide (550 mg, 0.83 mmol) in 5 ml THF/1-Methyl-2-pyrrolidinone (4:1) containing 48 mg of tetrakis(triphenylphosphine)palladium (0). The reaction mixture is stirred at room temp. for 1 h. 30 ml Dichloromethane (DCM) and 30 ml sat. NH_4Cl solution are

added. The organic phase is separated and the water phase is extracted twice with DCM. The combined organic fractions are dried with MgSO4, followed by filtration, evaporation of the solvents and flash-chromatography (Hexane/Ethylacetate; 3:2) to yield 5-(4-methoxyphenyl sulfonyl)-2-pyrid-2-yl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-carboxylic acid benzhydryloxy-amide.

Step B: 5-(4-methoxyphenylsulfonyl)-2-pyrid-2-yl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-hydroxamic acid

5-(4-methoxyphenylsulfonyl)-2-pyrid-2-yl-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-carboxylic acid benzhydryloxy-amide (200 mg, 0.33 mmol) treated in the same manner as 2-(methoxycarbonyl)-5-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-6-carboxylic acid benzhydryloxy-amide to afford 5-(4-methoxyphenylsulfonyl)-2-pyrid-2-yl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-hydroxamic acid: Cal. 445.4, found $(MH)^+$ 445.8.

Example 42



Preparation of 5-(4-methoxyphenylsulfonyl)-2-pyrid-2-yl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-hydroxamic acid

Step A: 5-(4-methoxyphenylsulfonyl)-2-pyrid-3-yl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-carboxylic acid benzhydryloxy-amide

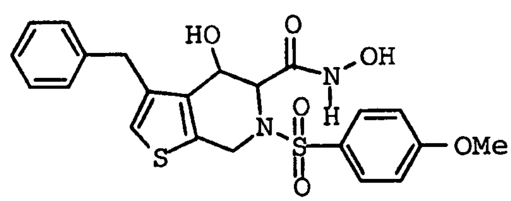
Utilizing 3-(tributylstannyl)pyridine, 5-(4-methoxy phenylsulfonyl)-2-pyrid-3-yl-4,5,6,7-tetrahydrothieno [3,2-c]pyridine-6-carboxylic acid benzhydryloxy-amide is prepared from 2-iodo-5-(4-methoxyphenylsulfonyl)-

4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-carboxylic acid benzhydryloxy-amide (250 mg, 0.38 mmol) in the same manner as 5-(4-methoxyphenylsulfonyl)-2-pyrid-2-yl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-carboxylic acid benzhydryloxy-amide. The product was purified by flash chromatography ($CHCl_3$/MeOH; 19:1).

Step B: 5-(4-methoxyphenylsulfonyl)-2-pyrid-3-yl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-hydroxamic acid

5-(4-Methoxyphenylsulfonyl)-2-pyrid-3-yl-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid was prepared from 5-(4-methoxyphenylsulfonyl)-2-pyrid-3-yl-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-carboxylic acid benzhydryloxy-amide (100 mg, 0.164 mmol) in the same manner as 5-(4-methoxyphenylsulfonyl)-2-pyrid-2-yl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-hydroxamic acid. The product was purified by preparative thin layer chromatography: Cal. 445.4, found $(MH)^+$ 446.0.

Example 43



Preparation of 4-Hydroxy-3-benzyl-4-hydroxy-6-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-5-hydroxamic acid

Step A: 2-Amino-3-(4-benzylthien-3-yl)-3-hydroxy-propionic acid

To 4-benzyl-thiophen-3-carboxaldeyde (3 g, 14.84 mmol) in 6 ml ethanol is added glycine (557 mg, 7.42 mmol) and the reaction is cooled to 0°C. A cold solution of KOH (832 mg, 14.84 mmol) in 4.5 ml ethanol is added in one shot. The reaction is stirred for 2 h at 0°C and then kept in a refrigerator over night. Hexane (50 ml) and

water (50 ml) are added and then 5 ml 1N HCl. A precipitate formed between the organic and the water phase. The suspension is filtered through a fritted glass funnel and the collected solid is washed with diethylether to yield 2-amino-3-(4-benzylthien-3-yl)-3-hydroxy-propionic acid: Cal. 278.3, found $(MH)^+$ 278.0.

Step B: 3-Benzyl-4-hydroxy-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-5-carboxylic acid

2-Amino-3-(4-benzylthien-3-yl)-3-hydroxy-propionic acid (880 mg, 3.17 mmol) is suspended in 25.4 ml of 0.25 N sulfuric acid and formaldehyde (2.57 ml, 12.33 M) was added. The mixture was stirred for 2 h at room temp. The reaction suspension is then filtered through a small fritted glass funnel and the obtained white powder is washed with diethylether and dried at high vacuum to yield 3-benzyl-4-hydroxy-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-5-carboxylic acid: Cal. 290.3, found $(MH)^+$ 290.2.

Step C: 3-Benzyl-4-hydroxy-6-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-5-carboxylic acid

3-Benzyl-4-hydroxy-4,5,6,7-tetrahydro-thieno[2,3-c] pyridine-5-carboxylic acid (642 mg, 1.9 mmol) is suspended in 8.54 ml of 1M Na_2CO_3-solution. 4-Methoxy benzenesulfonylchloride in 5 ml dioxane is added drop-wise at room temperature over a time period of 6 hours. The reaction suspension is stirred for another 6 h and is then transferred into a separator funnel and 100 ml water are added. The water phase is extracted twice with ethyl acetate. The aqueous layer is acidified (pH 0-1, 6N HCl) and the water phase is extracted three more times with ethyl acetate. The combined organic extracts are dried with $MgSO_4$ and the solvent is evaporated to give 3-benzyl-4-hydroxy-6-(4-methoxyphenylsulfonyl)-

4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-5-carboxylic acid as an oil: Cal. 458.5, found $(M-H)^-$ 458.2.

Step D: 4-Acetoxy-3-benzyl-4-hydroxy-6-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-5-carboxylic acid

3-Benzyl-4-hydroxy-6-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[2,3-c]pyridine-5-carboxylic acid (362 mg, 0.85 mmol) is acetylated with acetic anhydride as described above and is purified by flash-chromatography ($CDCl_3$/MeOH; 4:1) to yield 4-acetoxy-3-benzyl-4-hydroxy-6-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno [2,3-c]pyridine-5-carboxylic acid: Cal. 500.6, found $(M-H)^-$ 500.

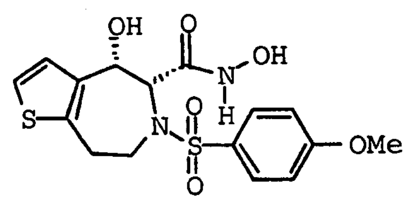
Step E: 4-Acetoxy-3-benzyl-4-hydroxy-6-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-5-hydroxamic acid

A solution of 4-acetoxy-3-benzyl-4-hydroxy-6-(4-methoxy phenylsulfonyl)-4,5,6,7-tetrahydro-thieno[2,3-c] pyridine-5-carboxylic acid (59 mg, 0.12 mmol) in 4 ml dichloromethane (DCM) is cooled to 0°C under an Argon blanket. Hydroxylamine hydrochloride salt (163 mg, 2.35 mmol) is added followed by the drop-wise addition of triethylamine (246µl, 1.76 mmol). Bromo-tris-pyrrolidino-phosphonium hexafluorophosphate (PyBrop) (83 mg, 2.35 mmol) is then added. The reaction is stirred at 0°C for 60 min. The solvents are evaporated and the residue is purified by preparative thin layer chromatography ($CHCl_3$/MeOH; 9:1) to yield 4-acetoxy-3-benzyl-4-hydroxy-6-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[2,3-c]pyridine-5-hydroxamic acid: Cal. 516.5, found $(MH)^+$ 515.2.

Step F: 4-Hydroxy-3-benzyl-4-hydroxy-6-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-5-hydroxamic acid

To 4-Acetoxy-3-benzyl-4-hydroxy-6-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-5-hydroxamic acid (40 mg, 0.097 mmol) in 2 ml methanol is added 600 µl of a 20% K_2CO_3-solution. The reaction is stirred at room temp. for 45 min. The product is purification by preparative thin layer chromatography ($CHCl_3$/ MeOH; 6:1) to afford 4-hydroxy-3-benzyl-4-hydroxy-6-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno [2,3-c]pyridine-5- hydroxamic acid: Cal. 475.5, found $(MH)^+$ 474.8; ^{1}H NMR (DMSO) δ 10.55 (s, 1H), 8.75 (s, 1H), 7.65 (d, 2H), 7.28 Hz (t, 2H), 7.2 (m, 1H), 7.1 (d, 2H), 7.05 (d, 2H), 6.65 (s, 1H), 5.7 (d, 1H), 4.62 (m, 3H), 4.5 (d, 1H), 3.9 (dd, 2H), 3.85 (s, 3H).

Example 44



Preparation of cis-(+/-)-4-Hydroxy-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid

Step A: Methyl (4-Methoxyphenylsulfonylamino)acetate

Glycine methyl ester hydrochloride (25 g, 0.2 mol) was dissolved in 200-mL of anhydrous methylene chloride. The solution was cooled to 0°C on ice. Triethylamine (40.5 g, 0.4 mol) was added and the solution allowed to stir for an additional 15 minutes. 4-Methoxybenzene sulfonyl chloride was added and the reaction allowed to warm slowly to room temperature and stir overnight. The reaction mixture was washed twice with 2M ammonium chloride then brine. The organic layer was dried over sodium sulfate, filtered, evaporated to dryness and purified by column chromatography (silica gel, 30% ethyl

acetate in hexanes) to yield the product as a white crystalline solid: MS: $(M+H)^+$ 260, $(M+NH_4)^+$ 277.

Step B: Methyl N-(2-(3-bromothien-2-yl)ethyl)-N-(4-methoxy phenylsulfonyl)aminoacetate

To a solution of 3-bromo-2-(2-hydroxyethyl)thiophene (2.07 g, 10 mmol) in THF (100 mL) was added methyl (4-methoxyphenylsulfonylamino)acetate (3 g, 11.6 mmol) and triphenylphosphine (3.18 g, 12.1 mmol). This solution was then cooled to 0°C and treated over 10 minutes with diisopropyl azodicarboxylate (2.37 mL, 12 mmol). The cooling bath was removed and the mixture was stirred for 24 hrs at 25°C. The solvent was removed in vacuo and the residue was reconstituted in ethyl acetate. The solution was then washed with saturated aqueous sodium bicarbonate, H_2O, and brine. The organic layer was dried (Na_2SO_4), concentrated, and purified by column chromatography (silica, 5% ethyl acetate in toluene) to give methyl N-(2-(3-bromothien-2-yl)ethyl)-N-(4-methoxy phenylsulfonyl)aminoacetate: MS: $(M+H)^+$ 448, 450, $(M+NH_4)^+$ 465, 467; ^1H NMR ($CDCl_3$) δ 7.78 (d, 2H), 7.14 (d, 1H), 6.96 (d, 2H), 6.9 (d, 1H), 4.06 (s, 2H), 3.87 (s, 3H), 3.65 (s, 3H), 3.46 (dd, 2H), 3.07 (d, 2H).

Step C: Methyl N-(4-methoxyphenylsulfonyl)-N-(2-(3-vinylthien-2-yl)ethyl)aminoacetate

Methyl N-(2-(3-bromothien-2-yl)ethyl)-N-(4-methoxy phenylsulfonyl)aminoacetate (1.86 g, 4.15 mmol) in toluene (28 mL) was treated with tributyl(vinyl)tin (3.1 mL, 10.6 mmol). The solution was heated to reflux for 5 minutes and then treated with dichlorbis(triphenyl phosphine)palladium (II) (250 mg, 0.36 mmol). The reaction mixture was stirred at reflux for 18 hrs and then cooled to 25°C. The mixture was diluted with diethyl ether and treated with 10% aqueous potassium fluoride for 30 minutes. Filtration through a plug of celite removed solids. The liquid phases of the

filtrate were separated and the organic layer was washed with 10% aqueous potassium fluoride, dried (Na_2SO_4) and concentrated. The tan oil was purified by flash chromatography (silica, 25 to 40% ethyl acetate in hexanes) to give methyl N-(4-methoxyphenylsulfonyl)-N-(2-(3-vinylthien-2-yl)ethyl)aminoacetate; ^1H NMR ($CDCl_3$) δ 7.75 (d, 2H), 7.13 (d, 1H), 7.05 (d, 1H), 6.94 (d, 2H), 6.64 (dd, 1H), 5.51 (dd, 1H), 5.21 (dd, 1H), 4.00 (s, 2H), 3.84 (s, 3H), 3.62 (s, 3H), 3.36 (dd, 2H), 3.11 (dd, 2H).

Step D: Methyl N-(2-(3-formylthien-2-yl)ethyl)-N-(4-methoxyphenylsulfonyl)aminoacetate

To a solution of methyl N-(4-methoxyphenylsulfonyl)-N-(2-(3-vinylthien-2-yl)ethyl)aminoacetate (0.195 g, 0.49 mmol) dissolved in THF and H_2O (4:1, 6 mL) was added a 2.5 wt.% solution of osmium tetroxide in 2-methyl-2-propanol (0.25 mL, 0.02 mmol) and sodium metaperiodate (130 mg, 0.6 mmol). The reaction mixture turned black and a white precipitate formed. The mixture was then treated with a second portion of sodium metaperiodate (130 mg, 0.6 mmol) and stirred for 30 minutes at 25 °C. The THF was then evaporated and the mixture was diluted with H_2O and the product was extracted into ethyl acetate. The organic layer was washed with brine, dried ($MgSO_4$), concentrated and purified by column chromatography (silica, 25 to 50% ethyl acetate in hexanes) to give methyl N-(2-(3-formylthien-2-yl)ethyl)-N-(4-methoxyphenylsulfonyl) aminoacetate: ^1H NMR ($CDCl_3$) δ 9.94 (s, 1H), 7.75 (d, 2H), 7.36 (d, 1H), 7.13 (d, 1H), 6.93 (d, 2H), 4.07 (s, 2H), 3.84 (s, 3H), 3.63 (s, 3H), 3.46 (s, 4H).

Step E: N-(2-(3-formylthien-2-yl)ethyl)-N-(4-methoxyphenylsulfonyl)aminoacetic acid

To a solution of methyl N-(2-(3-formylthien-2-yl)ethyl)-N-(4-methoxyphenylsulfonyl)aminoacetate (300 mg, 0.76

mmol) in THF (8 mL) at 0°C was added 1N aqueous KOH (1 mL, 1 mmol). The reaction mixture was allowed to warm to 25°C over 1.5 hrs and then the THF was removed in vacuo. Dilution with H_2O was followed by extraction with ethyl acetate and back extraction of the organic layer with 0.5N aqueous KOH. The combined aqueous layers were acidified with 1N aqueous HCl (to pH 2) to give a white precipitate that was extracted into ethyl acetate. The organic layer was dried (Na_2SO_4) and concentrated to give N-(2-(3-formylthien-2-yl)ethyl)-N-(4-methoxyphenyl sulfonyl)aminoacetic acid: ^{1}H NMR ($CDCl_3$) δ 9.91 (s, 1H), 7.73 (d, 2H), 7.35 (d, 1H), 7.13 (d, 1H), 6.93 (d, 2H), 4.10 (s, 2H), 3.83 (s, 3H), 3.46 (s, 4H).

Step F: tert-butyldimethylsilyl N-(2-(3-formylthien-2-yl)ethyl)-N-(4-methoxyphenylsulfonyl)aminoacetate

To a solution of N-(2-(3-formylthien-2-yl)ethyl)-N-(4-methoxyphenylsulfonyl)aminoacetic acid (260 mg, 0.68 mmol) dissolved in dichloromethane and N,N-dimethyl formamide (7:1, 5.7 mL) was added imidazole (56 mg, 0.82 mmol) and tert-butyldimethylsilyl chloride (124 mg, 0.82 mmol). The reaction mixture was allowed to stir at 25°C for 1.33 hrs, a white precipitate formed. This mixture was diluted with diethyl ether and washed with saturated aqueous potassium bisulfate, saturated aqueous sodium bicarbonate, and brine. The organic phase was dried (Na_2SO_4), concentrated, and co-distilled with toluene to give tert-butyldimethylsilyl N-(2-(3-formylthien-2-yl) ethyl)-N-(4-methoxyphenylsulfonyl)aminoacetate, which was carried to the next step without further purification: ^{1}H NMR ($CDCl_3$) δ 9.95 (s, 1H), 7.74 (d, 2H), 7.36 (d, 1H), 7.12 (d, 1H), 6.92 (d, 2H), 4.04 (s, 2H), 3.83 (s, 3H), 3.48 (m, 4H), 0.89 (s, 9H), 0.21 (2, 6H).

Step G: cis-(+/-)-4-(tert-butyldimethylsilanyloxy)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-

thieno[2,3-d]azepine-5-carboxylic acid and trans-(+/-)-4-(tert-butyldimethylsilanyloxy)-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylic acid

To a solution of crude tert-butyldimethylsilyl N-(2-(3-formylthien-2-yl)ethyl)-N-(4-methoxyphenylsulfonyl)amino acetate (313 mg, 0.63 mmol) in THF (5 mL) at -78°C was added dropwise a 0.5 M solution of KHMDS in toluene (1.4 mL, 0.7 mmol). The reaction mixture was slowly warmed to -60°C over 1.5 hrs and then diluted with ethyl acetate. This mixture was poured onto a 1 to 1 mixture of H_2O and saturated aqueous ammonium chloride. After separation the organic layer was washed with H_2O and brine, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (silica, 2.5 to 10% methanol in methylene chloride) to give cis-(+/-)-4-(tert-butyldimethylsilanyloxy)-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylic acid and trans-(+/-)-4-(tert-butyldimethyl silanyloxy)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylic acid: MS(cis): $(M+H)^+$ 498, $(M+NH_4)^+$ 515 and MS(trans): $(M+H)^+$ 498, $(M+NH_4)^+$ 515.

Step H: cis-(+/-)-4-(tert-butyldimethylsilanyloxy)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid

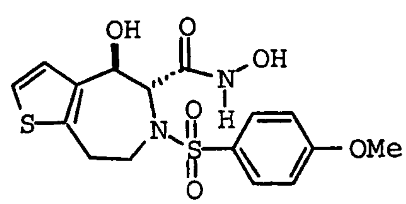
A solution of cis-(+/-)-4-(tert-butyldimethyl silanyloxy)-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylic acid (50 mg, 0.1 mmol) in CH_2Cl_2 (2 mL) at 0°C was treated sequentially with hydroxylamine hydrochloride (22 mg, 0.32 mmol), diisopropylethylamine (72 µL, 0.41 mmol), and PyBroP (57 mg, 0.12 mmol). The mixture was allowed to warm to 25°C over 2 hrs and was then concentrated. The residue was dissolved in ethyl acetate and the remaining solids were filtered off through a plug of

cotton. The filtrate was washed with brine, 1N aqueous HCl, and brine again. The organic phase was then dried (Na_2SO_4), concentrated, and purified by column chromatography (silica, 2.5% methanol in methylene chloride) to give cis-(+/-)-4-(tert-butyldimethyl silanyloxy)-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid: MS(cis): $(M-H)^-$ 511.

<u>Step I: cis-(+/-)-4-Hydroxy-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid</u>

To a stirred solution of crude cis-(+/-)-4-(tert-butyl dimethylsilanyloxy)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid (43 mg, 0.084 mmol) dissolved in THF (3 mL) at 0°C was added a 1 M solution of TBAF in THF (0.17 mL, 0.17 mmol). The reaction mixture was stirred for 15 minutes and then diluted with ethyl acetate. This solution was washed with 1 M aqueous HCl and H_2O, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography (silica, 2.5 to 10% methanol in methylene chloride) to give cis-(+/-)-4-Hydroxy-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid: MS(cis): $(M-H)^-$ 397.

<u>Example 45</u>

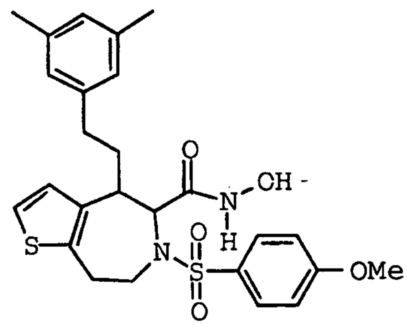


<u>Preparation of trans-(+/-)-4-Hydroxy-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid</u>

trans-(+/-)-4-Hydroxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic

acid was prepared from trans-(+/-)-4-(tert-butyldimethyl silanyloxy)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylic acid in the same manner as cis-(+/-)-4-Hydroxy-6-(4-methoxy phenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid: MS: $(M+NH_4)^+$ 416.

Example 46



Preparation of trans-(+/-)-4-(2-(3,5-Dimethylphenyl) ethyl)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid

Step A: Methyl N-(2-{3-(3-(tert-butyldimethylsilanyl oxy)propenyl)thien-2-yl}ethyl)-N-(4-methoxyphenyl sulfonyl)aminoacetate

Methyl N-(2-(3-bromothien-2-yl)ethyl)-N-(4-methoxy phenylsulfonyl)aminoacetate (4.83 g, 10.8 mmol) in toluene (65 mL) was treated with (Z)-1-(tri-n-butyl stannyl)-3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-1-propene (5.8 g, 12.6 mmol). This solution was heated to reflux for 5 minutes and then treated with dichlorbis (triphenylphosphine)palladium (II) (605 mg, 0.86 mmol). The reaction mixture was stirred at reflux for 2 hrs and then cooled to 25°C. The mixture was diluted with diethyl ether and treated with 10% aqueous potassium fluoride for 1 hr. Filtration through a plug of celite removed the solids. The liquid phases of the filtrate were separated and the organic layer was washed with 10% aqueous potassium fluoride, dried (Na_2SO_4) and

concentrated. The tan oil was purified by flash chromatography (silica, 10 to 25% ethyl acetate in hexanes) to give Methyl N-(2-{3-(3-(tert-butyldimethyl silanyloxy)propenyl)thien-2-yl}ethyl)-N-(4-methoxyphenyl sulfonyl)aminoacetate: ^{1}H NMR ($CDCl_3$) δ 7.78 (d, 2H), 7.09 (d, 1H), 6.96 (d, 2H), 6.89 (d, 1H), 6.29 (m, 1H), 5.76 (m, 1H), 4.33 (dd, 2H), 4.02 (s, 2H), 3.87 (s, 3H), 3.64 (s, 3H), 3.38 (m, 2H), 3.06 (m, 2H).

Step B: N-(2-{3-(3-(tert-butyldimethylsilanyl oxy)propenyl)thien-2-yl}ethyl)-N-(4-methoxyphenyl sulfonyl)aminoacetic acid

To a stirred solution of methyl N-(2-{3-(3-(tert-butyl dimethylsilanyloxy)propenyl)thien-2-yl}ethyl)-N-(4-methoxyphenylsulfonyl)aminoacetate (4.33 g, 8 mmol) in THF (80 mL) at 0°C was added 1 N LiOH (12 mL). The reaction mixture was allowed to warm to 25°C and was stirred for 3 hrs. The THF was removed under reduced pressure and the reaction mixture was diluted with water and acidified with 1N aqueous HCl (12 mL). The white precipitate was extracted into ethyl acetate (2x) and the combined organic layers were dried (Na_2SO_4) and concentrated to give crude N-(2-{3-(3-(tert-butyl dimethylsilanyl oxy)propenyl)thien-2-yl}ethyl)-N-(4-methoxyphenylsulfonyl)aminoacetic acid, which was carried onto the next step without purification: ^{1}H NMR ($CDCl_3$) δ 7.77 (d, 2H), 7.10 (d, 1H), 6.96 (d, 2H), 6.86 (d, 1H), 6.29 (m, 1H), 5.76 (m, 1H), 4.33 (d, 2H), 4.00 (s, 2H), 3.87 (s, 3H), 3.41 (m, 2H), 3.06 (m, 2H).

Step C: N-(2-{3-(3-hydroxypropenyl)thien-2-yl}ethyl)-N-(4-methoxyphenylsulfonyl)aminoacetic acid

To a stirred solution of crude N-(2-{3-(3-(tert-butyl dimethylsilanyloxy)propenyl)thien-2-yl}ethyl)-N-(4-methoxyphenylsulfonyl)aminoacetic acid (4.4 g, 8 mmol) in THF (70 mL) at 0°C was added a 1 M solution of TBAF in THF (16 mL, 16 mmol). The reaction mixture was

allowed to warm to 25°C and was stirred for 5 hrs. The THF was removed under reduced pressure and the residue was redissolved in ethyl acetate. This solution was washed with 1N aqueous HCl, water, and brine. The organic phase was then dried (Na_2SO_4) and concentrated to give a tan oil, which solidified upon trituration with diethyl ether. The solid product was collected and rinsed with cold diethyl ether to give N-(2-{3-(3-hydroxypropenyl) thien-2-yl}ethyl)-N-(4-methoxyphenyl sulfonyl)aminoacetic acid: ^1H NMR ($CDCl_3$) δ 7.75 (d, 2H), 7.11 (d, 1H), 6.96 (d, 2H), 6.85 (d, 1H), 6.38 (d, 1H), 5.84 (m, 1H), 4.29 (d, 2H), 3.95 (s, 2H), 3.86 (s, 3H), 3.43 (m, 2H), 3.07 (m, 2H).

<u>Step D: 10-(4-methoxyphenylsulfonyl)-9,10,11,12-tetra hydro-6H-7-oxa-1-thia-10-aza-cyclopentacycloundecen-8-one</u>

A solution of N-(2-{3-(3-hydroxypropenyl)thien-2-yl} ethyl)-N-(4-methoxyphenylsulfonyl)aminoacetic acid (1.45 g, 3.5 mmol) in acetonitrile (25 mL) was treated with triethylamine (3.9 mL, 28.1 mmol). This solution was slowly added (15 hrs, via syringe pump) to a solution of 2-chloro-1-methylpyridinium iodide in acetonitrile (500 mL) heated at reflux. The reaction mixture was heated another 5 hrs at reflux and then the acetonitrile was evaporated. The residue was suspended in ethyl acetate and the solid by-products were removed via filtration. The filtrate was concentrated and the crude product was purified by flash chromatography (silica, 25 to 40% ethyl acetate in hexanes) to give 10-(4-methoxyphenyl sulfonyl)-9,10,11,12-tetrahydro-6H-7-oxa-1-thia-10-aza-cyclopentacycloundecen-8-one: MS: $(M+H)^+$ 394, $(M+NH_4)^+$ 411.

<u>Step E: tert-butyldimethylsilyl cis-(+/-)-6-(4-methoxy phenylsulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate and cis-(+/-)-6-(4-</u>

methoxyphenyl sulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4H-thieno[2,3-d] azepine-5-carboxylic acid

To a solution of 10-(4-methoxyphenylsulfonyl)-9,10,11,12-tetrahydro-6H-7-oxa-1-thia-10-aza-cyclopentacycloundecen-8-one (1.31 g, 3.3 mmol) in THF (33 mL) at -78°C was added TBSOTf (0.8 mL, 3.5 mmol) followed immediately by a 0.5 M solution of KHMDS in toluene (7 mL, 3.5 mmol). The cooling bath was then removed and the reaction mixture was allowed to warm to 25°C, over 30 minutes. This room temperature mixture was then heated to reflux for 4 hrs. The mixture was cooled to 25°C and poured onto a mixture of ethyl acetate and saturated aqueous NH_4Cl. The layers were separated and the organic phase was washed with H_2O and brine and then dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography (silica, 25 to 50% ethyl acetate in hexanes followed by 5 to 10% methanol in methylene chloride) to give tert-butyl dimethylsilyl cis-(+/-)-6-(4-methoxyphenylsulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate: ^1H NMR ($CDCl_3$) δ 7.74 (d, 2H), 6.99-6.90 (m, 3H), 6.81 (d, 1H), 6.47 (m, 1H), 5.27 (d, 1H), 5.23 (d, 1H), 4.90 (d, 1H), 4.02-3.95 (m, 2H), 3.85 (s, 3H), 3.55 (m, 1H), 3.13 (m, 1H), 2.94 (m, 1H), 0.84 (s, 9H), 0.07 (s, 3H), 0.04 (s, 3H); and cis-(+/-)-6-(4-methoxy phenylsulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4H-thieno [2,3-d]azepine-5-carboxylic acid: MS: $(M+H)^+$ 394, $(M+NH_4)^+$ 411.

Step F: cis-(+/-)-6-(4-methoxyphenylsulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylic acid

To a solution of tert-butyldimethylsilyl cis-(+/-)-6-(4-methoxyphenylsulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate (72 mg, 0.14 mmol) in methanol and THF (3:1, 2.4 mL) at 0°C was added a solution of K_2CO_3 (60 mg, 0.43 mmol) in H_2O (0.6 mL).

The cloudy reaction mixture was allowed to warm to 25°C over 30 minutes and was then concentrated to 1/4th of the original volume. Dilution with H_2O and acidification with 1N HCl (to pH 2) gave a white precipitate that was extracted into ethyl acetate. The organic phase was dried (Na_2SO_4) and concentrated to give cis-(+/-)-6-(4-methoxyphenylsulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylic acid (57 mg, 0.14 mmol), which was carried to the next step without further purification: MS: $(M+H)^+$ 394, $(M+NH_4)^+$ 411.

Step G: Methyl cis-(+/-)-6-(4-methoxyphenylsulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate

To a solution of crude cis-(+/-)-6-(4-methoxyphenyl sulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4H-thieno[2,3-d] azepine-5-carboxylic acid (53 mg, 0.13 mmol) in benzene, methylene chloride and methanol (3:2:2, 1.75 mL) at 0°C was added a 2 M solution of $TMSCHN_2$ (0.135 mL, 0.27 mmol) in hexanes. The reaction mixture was stirred 15 minutes and then the solvents were removed under reduced pressure to give methyl cis-(+/-)-6-(4-methoxyphenyl sulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate as a clear oil: MS: $(M+H)^+$ 408, $(M+NH_4)^+$ 425.

Step H: Methyl cis-(+/-)-4-(2-(3,5-dimethylphenyl) ethyl)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate

To a solution of methyl cis-(+/-)-6-(4-methoxyphenyl sulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4H-thieno[2,3-d] azepine-5-carboxylate (55 mg, 0.13 mmol) in THF (1.25 mL) at 0°C was added a 0.5 M solution of 9-BBN (0.5 mL, 0.25 mmol) in THF. The reaction mixture was allowed to warm to 25°C over 4 hrs and was then treated sequentially with $PdCl_2(dppf)\cdot CH_2Cl_2$ (16 mg, 0.02 mmol),

5-iodo-m-xylene (0.15 mL, 1 mmol), K_2CO_3 (86 mg, 0.62 mmol), DMF (1 mL), and H_2O (0.1 mL). After stirring 5 minutes at 25°C, the solution was diluted with diethyl ether and washed with H_2O, 1N aqueous HCl, saturated aqueous $NaHCO_3$, and brine. The organic layer was dried (Na_2SO_4), concentrated, and purified by column chromatography (silica, 3% ethyl acetate in toluene) to give methyl cis-(+/-)-4-(2-(3,5-dimethylphenyl)ethyl)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno [2,3-d]azepine-5-carboxylate: MS: $(M+H)^+$ 514, $(M+NH_4)^+$ 531.

<u>Step I: trans-(+/-)-4-(2-(3,5-dimethylphenyl)ethyl)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylic acid</u>

To a solution of methyl cis-(+/-)-4-(2-(3,5-dimethyl phenyl)ethyl)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate (25 mg, 0.049 mmol) in THF and H_2O (3:1, 2 mL) was added 1N aqueous LiOH (0.25 mL, 0.25 mmol). The reaction mixture was heated to reflux for 7 hrs and then the THF was removed in vacuo. Dilution with H_2O followed by acidification with 1N aqueous HCl gave a white precipitate that was extracted into ethyl acetate. The organic layer was then washed with H_2O and brine, dried (Na_2SO_4) and concentrated to give the crude trans-(+/-)-4-(2-(3,5-dimethylphenyl)ethyl)-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylic acid: MS: $(M-H)^-$ 498.

<u>Step J: trans-(+/-)-4-(2-(3,5-dimethylphenyl)ethyl)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid</u>

A solution of trans-(+/-)-4-(2-(3,5-dimethylphenyl) ethyl)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylic acid (23 mg, 0.046 mmol) in CH_2Cl_2 (1.5 mL) at 0°C was treated sequentially

with hydroxylamine hydrochloride (10 mg, 0.14 mmol), diisopropylethylamine (35 µL, 0.2 mmol), and PyBroP (26 mg, 0.056 mmol). The mixture was allowed to warm to 25°C over 2.5 hrs and was then concentrated. The residue was dissolved in ethyl acetate and the remaining solids were removed via filtration. The filtrate was washed with brine, 1N aqueous HCl, and brine again. The organic phase was then dried (Na_2SO_4), concentrated, and purified by column chromatography (silica, 2.5% methanol in methylene chloride) to give trans-(+/-)-4-(2-(3,5-dimethylphenyl)ethyl)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid: MS: $(M+H)^+$ 515, $(M+NH_4)^+$ 532.

Example 47

Preparation of Methyl trans-(+/-)-6-(4-methoxyphenyl sulfonyl)-4-(3-methylbutyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate

To a solution of methyl trans-(+/-)-6-(4-methoxyphenyl sulfonyl)-4-(3-methylbut-3-enyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate (39 mg, 0.087 mmol) in benzene (1 mL) was added chlorotris(triphenyl phosphine)rhodium(I) (16 mg, 0.017 mmol). The reaction flask was evacuated and flushed with nitrogen (3X) and hydrogen (3X) each, and finally stirred under an atmosphere of hydrogen gas for 3 hrs. The solvent was evaporated in vacuo and the residue was purified by column chromatography (silica, 15 to 25% ethyl acetate in hexanes) to give methyl trans-(+/-)-6-(4-methoxy phenylsulfonyl)-4-(3-methylbutyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate: MS: $(M+H)^+$ 452, $(M+NH_4)^+$ 469.

Example 48

Preparation of Methyl trans-(+/-)-4-(2-{3-(hydroxy methyl)phenyl}ethyl)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate

Methyl trans-(+/-)-4-(2-(3-formylphenyl)ethyl)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate in THF at 0°C was treated with sodium borohydride to give methyl trans-(+/-)-4-(2-{3-(hydroxymethyl)phenyl}-ethyl)-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate: MS: $(M+H)^+$ 516, $(M+NH_4)^+$ 533.

Example 49

Utilizing the procedures of Examples 1-48, the compounds of Table I were prepared.

TABLE I

trans-(+/-)-6-(4-methoxyphenylsulfonyl)-4-phenethyl-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid: MS $(M+H)^+$ 487, $(M+NH_4)^+$ 504.

trans-(+/-)-6-(4-methoxyphenylsulfonyl)-4-[2-(4-trifluoromethylphenyl)ethyl]-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid: MS $(M-H)^-$ 553.

trans-(+/-)-4-[2-(4-chlorophenyl)ethyl]-6-(4-methoxy phenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d] azepine-5-hydroxamic acid: MS $(M+H)^+$ 521 and 523, $(M+NH_4)^+$ 538 and 540.

trans-(+/-)-6-(4-methoxyphenylsulfonyl)-4-[2-(4-methoxy phenyl)ethyl]-5,6,7,8-tetrahydro-4H-thieno[2,3-d] azepine-5-hydroxamic acid: MS $(M+H)^+$ 517, $(M+NH_4)^+$ 534.

trans-(+/-)-6-(4-methoxyphenylsulfonyl)-4-[2-(3-methoxy phenyl)ethyl]-5,6,7,8-tetrahydro-4H-thieno[2,3-d] azepine-5-hydroxamic acid: MS $(M+H)^+$ 517, $(M+NH_4)^+$ 534.

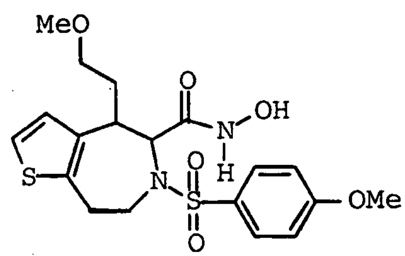
E-trans-(+/-)-6-(4-methoxyphenylsulfonyl)-4-(4-phenyl but-3-enyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid: MS $(M+H)^+$ 513, $(M+NH_4)^+$ 530.

trans-(+/-)-6-(4-methoxyphenylsulfonyl)-4-(3-methylbut-3-enyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid: MS $(M+H)^+$ 451, $(M+NH_4)^+$ 468.

trans-(+/-)-6-(4-methoxyphenylsulfonyl)-4-(3-methyl butyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid: MS $(M+H)^+$ 453, $(M+NH_4)^+$ 470.

trans-(+/-)-4-[2-(3-hydroxymethylphenyl)ethyl]-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid: MS $(M+H)^+$ 517, $(M+NH_4)^+$ 534.

Example 50



Preparation of trans-(+/-)-6-(4-methoxyphenylsulfonyl)-4-(2-methoxyethyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid

Step A: Methyl cis-(+/-)-4-(2-hydroxyethyl)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate and 6-(4-methoxyphenylsulfonyl)-5,6,6a,9,10,10a-hexahydro-4H-8-oxa-3-thia-6-aza-benz[e]azulen-7-one

To a solution of methyl cis-(+/-)-6-(4-methoxyphenyl sulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate (39 mg, 0.096 mmol) in THF (2 mL) at 0°C was added a 0.5 M solution of 9-BBN (0.38 mL, 0.19 mmol) in THF. The reaction mixture was allowed to warm to 25°C over 2.5 hrs and was then cooled to 0°C. This solution was slowly treated with H_2O (1 mL) followed by $NaBO_3 \cdot 4H_2O$ and stirred 2.5 hrs. The mixture was then poured onto a solution of cold brine and diluted with diethyl ether. After separation, the organic phase was washed with H_2O and brine, dried (Na_2SO_4), concentrated, and purified by column

chromatography (silica, 50 to 75% ethyl acetate in hexanes) to give the higher Rf 6-(4-methoxyphenyl sulfonyl)-5,6,6a,9,10,10a-hexahydro-4H-8-oxa-3-thia-6-aza-benz[e]azulen-7-one: MS: $(M+H)^+$ 394, $(M+NH_4)^+$ 411; and the lower Rf methyl cis-(+/-)-4-(2-hydroxyethyl)-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate: MS: $(M+H)^+$ 426, $(M+NH_4)^+$ 443.

Step B: Methyl cis-(+/-)-6-(4-methoxyphenylsulfonyl)-4-(2-methoxyethyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate

To a vigorously stirred solution of crude methyl cis-(+/-)-4-(2-hydroxyethyl)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate (45 mg, 0.106 mmol) in methylene chloride (1 mL) at 0°C was added a 48% aqueous solution of HBF_4 (15 µL, 0.11 mmol). The mixture was treated with a 2 M solution of $TMSCHN_2$ (0.4 mL, 0.8 mmol) in hexanes until TLC (silica, 50% ethyl acetate in hexanes) anlysis indicated the starting material had been consumed. The reaction mixture was stirred a total of 1.5 hrs and was then diluted with methylene chloride. This mixture was washed with H_2O (3X), dried (Na_2SO_4), concentrated, and purified by column chromatography (silica, 25 to 37.5% ethyl acetate in hexanes) to give methyl cis-(+/-)-6-(4-methoxy phenylsulfonyl)-4-(2-methoxyethyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate: MS: $(M+H)^+$ 440, $(M+NH_4)^+$ 457.

Step C: trans-(+/-)-6-(4-methoxyphenylsulfonyl)-4-(2-methoxyethyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylic acid

To a solution of methyl cis-(+/-)-6-(4-methoxyphenyl sulfonyl)-4-(2-methoxyethyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate (41 mg, 0.09 mmol) dissolved in THF and H_2O (3:1, 2 mL) was added 1N LiOH

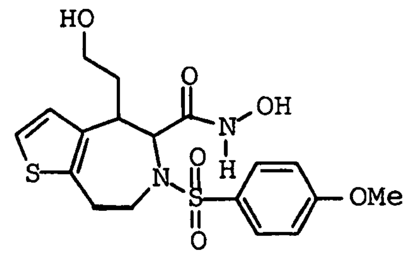
(0.27 mL, 0.27 mmol). The reaction mixture was heated to reflux for 14 hrs and then the THF was removed in vacuo. Dilution with H_2O followed by acidification with 1N aqueous HCl gave a white precipitate that was extracted into ethyl acetate. The organic layer was then washed with H_2O and brine, dried (Na_2SO_4) and concentrated to give crude trans-(+/-)-6-(4-methoxy phenylsulfonyl)-4-(2-methoxyethyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylic acid: MS: $(M+H)^+$ 426, $(M+NH_4)^+$ 443.

Step D: trans-(+/-)-6-(4-methoxyphenylsulfonyl)-4-(2-methoxyethyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid

A solution of trans-(+/-)-6-(4-methoxyphenylsulfonyl)-4-(2-methoxyethyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d] azepine-5-carboxylic acid (34 mg, 0.08 mmol) in CH_2Cl_2 (2 mL) at 0°C was treated sequentially with hydroxylamine hydrochloride (18 mg, 0.26 mmol), diisopropylethylamine (57 μL, 0.33 mmol), and PyBroP (45 mg, 0.097 mmol). This mixture was allowed to warm to 25°C over 1.5 hrs and was then concentrated. The residue was dissolved in ethyl acetate and the remaining solids were removed via filtration. The filtrate was washed with brine, 1 N HCl, and brine again. The organic phase was then dried (Na_2SO_4), concentrated, and purified by column chromatography (silica, 2.5% methanol in methylene chloride) to give trans-(+/-)-6-(4-methoxyphenyl sulfonyl)-4-(2-methoxyethyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid: MS: $(M-H)^-$ 439.

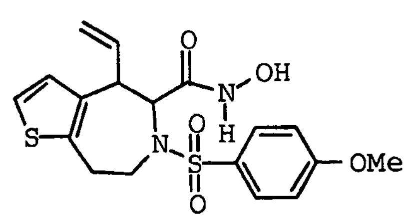
Example 51

Preparation of cis-(+/-)-4-[2-hydroxyethyl]-6-(4-methoxy phenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid



To a solution of 6-(4-methoxyphenylsulfonyl)-5,6,6a,9,10,10a-hexahydro-4H-8-oxa-3-thia-6-aza-benz[e]azulen-7-one (15 mg, 0.038 mmol) in dichloroethane (0.7 mL) was added hydroxylamine hydrochloride (13 mg, 0.19 mmol), diisopropylethylamine (35 µL, 0.2 mmol), and N,N-dimethylformamide (3 drops). The reaction mixture was heated to reflux for 8 hrs and then treated with additional quantities of hydroxylamine hydrochloride (25 mg, 0.36 mmol) and diisopropylethyl amine (70 µL, 0.4 mmol) at reflux. The mixture was stirred another 1 hr at reflux and then concentrated to remove the dichloroethane. The residue was dissolved in ethyl acetate and washed with H_2O, 1 M aqueous HCl, and brine. The organic phase was dried (Na_2SO_4), concentrated, and purified by column chromatography (silica, 1:10:190 acetic acid:methanol:methylene chloride) to give a mixture of higher Rf cis and trans-(+/-)-4-[2-hydroxy ethyl]-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylic acids and the lower Rf cis-(+/-)-4-[2-hydroxyethyl]-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid: MS: $(M-H)^-$ 425.

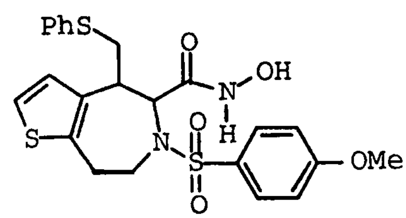
Example 52



Preparation of cis-(+/-)-6-(4-methoxyphenylsulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid

A solution of cis-(+/-)-6-(4-methoxyphenylsulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylic acid (17 mg, 0.043 mmol) in CH_2Cl_2 (1 mL) at 0°C was treated sequentially with hydroxylamine hydrochloride (9 mg, 0.13 mmol), diisopropylethylamine (30 μL, 0.17 mmol), and PyBroP (25 mg, 0.054 mmol). This mixture was allowed to warm to 25°C over 5 hrs and was then concentrated. The residue was dissolved in ethyl acetate and the remaining solids were removed via filtration. The filtrate was washed with brine, 1 M aqueous HCl, and brine again. The organic phase was then dried (Na_2SO_4), concentrated, and purified by column chromatography (silica, 5 to 10% methanol in methylene chloride to 1:10:90 acetic acid:methanol:methylene chloride) to give cis-(+/-)-6-(4-methoxyphenylsulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid: MS: $(M-H)^-$ 407.

Example 53



Preparation of trans-(+/-)-6-(4-methoxyphenylsulfonyl)-4-(phenylsulfanylmethyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid

Step A: cis-(+/-)-1-hydroxymethyl-6-(4-methoxyphenyl sulfonyl)-1,3a,4,5,6,9b-hexahydro-2-oxa-7-thia-4-aza-cyclopenta[e]azulen-3-one

To a solution of methyl cis-(+/-)-6-(4-methoxyphenyl sulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate (805 mg, 2 mmol) in THF and H_2O

(2:1, 10 mL) was added a 2.5 wt.% solution of osmium tetroxide in 2-methyl-2-propanol (0.32 mL, 0.026 mmol) and 4-methylmorpholine N-oxide (360 mg, 3.1 mmol). The reaction mixture was stirred for 20 hrs at 25°C. The THF was then evaporated and the mixture was diluted with H_2O. The excess oxidant was reduced with a 0.4 M aqueous solution of Na_2SO_3 (50 mL) and the product was extracted into ethyl acetate. The organic layer was washed with brine, dried (Na_2SO_4), concentrated and purified by column chromatography (silica, 50 to 75% ethyl acetate in hexanes) to give a higher Rf diasteriomer of cis-(+/-)-1-hydroxymethyl-6-(4-methoxyphenylsulfonyl)-1,3a,4,5,6,9b-hexahydro-2-oxa-7-thia-4-aza-cyclopenta[e]azulen-3-one: MS: $(M+H)^+$ 410, $(M+NH_4)^+$ 427; and a lower Rf diasteriomer of cis-(+/-)-1-hydroxymethyl-6-(4-methoxyphenylsulfonyl)-1,3a,4,5,6,9b-hexahydro-2-oxa-7-thia-4-aza-cyclopenta[e]azulen-3-one: ^1H NMR ($CDCl_3$) δ 7.66 (d, 2H), 7.05 (d, 1H), 6.90 (d, 2H), 6.66 (d, 1H), 5.46 (d, 1H), 4.74 (m, 1H), 4.21 (dd, 1H), 3.86 (s, 3H), 3.81 (dd, 1H), 3.58 (m, 1H), 3.49 (m, 1H), 3.35 (m, 1H), 2.88 (m, 2H), 1.55 (m, 1H).

Step B: cis-(+/-)-4-(1,2-dihydroxyethyl)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylic acid

To a solution of cis-(+/-)-1-hydroxymethyl-4-(4-methoxyphenylsulfonyl)-1,3a,4,5,6,9b-hexahydro-2-oxa-7-thia-4-aza-cyclopenta[e]azulen-3-one, a mixture of diastereomers, (375 mg, 0.92 mmol) in THF and H_2O (3:1, 12 mL) at 0°C was added 1N aqueous LiOH (2.25 mL, 2.25 mmol). The reaction mixture was stirred 15 minutes and then the THF was removed in vacuo. Dilution with H_2O followed by acidification with 2 M aqueous HCl (to pH 2) gave a white precipitate that was extracted into ethyl acetate (2X). The organic layers were combined and washed with H_2O and brine. The ethyl acetate phase was then dried (Na_2SO_4) and concentrated to give crude cis-

(+/-)-4-(1,2-dihydroxyethyl)-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylic acid: ^{1}H NMR (DMSO-d_6) δ 12.55 (bs, 1H), 7.73 (d, 2H), 7.11 (d, 1H), 7.05 (d, 2H), 6.82 (d, 1H), 5.56 (d, 1H), 4.55 (m, 1H), 4.26 (m, 1H), 3.87 (m, 1H), 3.80 (s, 3H), 3.51 (m, 1H), 3.35-3.17 (m, 2H), 3.01 (d, 1H), 2.84 (dd, 1H), 2.69 (m, 1H). The crude product could be crystallized from methylene chloride to give a pure white solid, free of residual acid, which can induce relactonization in subsequent steps.

Step C: (+/-)-1-hydroxy-4-(4-methoxyphenylsulfonyl)-1,3a,4,5,6,9b-hexahydro-2-oxa-7-thia-4-aza-cyclopenta[e]azulen-3-one

To a solution of cis-(+/-)-4-(1,2-dihydroxyethyl)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylic acid, a single diastereomer, (37 mg, 0.087 mmol) dissolved in THF (1 mL) at 0°C was added a 0.38 M solution of sodium metaperiodate (0.5 mL, 0.19 mmol) in H_2O. After 5 minutes a white precipitate formed. The reaction mixture was stirred a total of 15 minutes and then concentrated. The residue was poured onto a mixture of ethyl acetate and H_2O and then separated. The organic layer was washed with brine, dried (Na_2SO_4) and concentrated to give (+/-)-1-hydroxy-4-(4-methoxyphenylsulfonyl)-1,3a,4,5,6,9b-hexahydro-2-oxa-7-thia-4-aza-cyclopenta[e]azulen-3-one as a 4 to 1 mixture: ^{1}H NMR ($CDCl_3$, data only given for the major isomer) δ 7.71 (d, 2H), 7.07 (d, 1H), 6.92 (d, 2H), 6.79 (d, 1H), 5.73 (s, 1H), 5.60 (d, 1H), 4.19 (bs, 1H), 3.96 (d, 1H), 3.86 (s, 3H), 3.85 (m, 1H), 3.48 (m, 1H), 3.00-2.88 (m, 2H).

Step D: cis-(+/-)-4-hydroxymethyl-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylic acid

To a solution of 1-hydroxy-4-(4-methoxyphenylsulfonyl)-1,3a,4,5,6,9b-hexahydro-2-oxa-7-thia-4-aza-cyclopenta[e]azulen-3-one (as a 4 to 1 mixture of lactols) (30 mg, 0.076 mmol) in THF (1.5 mL) at 0°C was added sodium borohydride (4 mg, 0.1 mmol). The reaction mixture was stirred 30 minutes and then concentrated. The residue was reconstituted in ethyl acetate and washed with 1N aqueous HCl and H_2O. The organic layer was then dried (Na_2SO_4) and concentrated to give a 10 to 1 mixture of cis-(+/-)-4-hydroxymethyl-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylic acid and the corresponding γ-lactone: MS: $(M+H)^+$ 398, $(M+NH_4)^+$ 415.

Step E: Methyl cis-(+/-)-4-hydroxymethyl-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate

To a solution of the 10 to 1 mixture of cis-(+/-)-4-hydroxymethyl-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylic acid and the corresponding γ-lactone (30 mg, 0.076 mmol) in benzene and methanol (2:1, 1.5 mL) at 0°C was added a 2 M solution of $TMSCHN_2$ (0.1 mL, 0.2 mmol) in hexanes. The reaction mixture was stirred 15 minutes and then the solvents were removed under reduced pressure to give a 5 to 1 mixture of methyl cis-(+/-)-4-hydroxymethyl-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate and the corresponding γ-lactone: ^1H NMR ($CDCl_3$) δ 7.78 (d, 2H), 6.98 (d, 1H), 6.96 (d, 2H), 6.81 (d, 1H), 5.35 (d, 1H), 4.34-4.20 (m, 2H), 4.05 (m, 1H), 3.86 (s, 3H), 3.47 (m, 1H), 3.40 (s, 3H), 3.34 (m, 1H), 3.11 (m, 1H), 2.94 (dd, 1H), 1.95 (dd, 1H).

Step F: Methyl cis-(+/-)-6-(4-methoxyphenylsulfonyl)-4-phenylsulfanylmethyl-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate and methyl trans-(+/-)-6-(4-

methoxyphenylsulfonyl)-4-phenylsulfanylmethyl-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate

To a solution of the 5 to 1 mixture of methyl (+/-)-4-hydroxymethyl-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate and the corresponding γ-lactone (40 mg, 0.097 mmol) in THF (1 mL) was added diphenyl sulfide (62 mg, 0.28 mmol) and tri-n-butylphosphine (0.1 mL, 0.4 mmol). The solution was stirred 15 hrs at 25°C. TLC analysis (50% ethyl acetate in hexanes) indicated residual starting materials present so the mixture was heated to reflux and additional quantities of diphenyl sulfide (40 mg, 0.18 mmol) and tri-n-butylphosphine (0.05 mL, 0.2 mmol) were added. The reaction mixture was heated at reflux for 8 hrs and then cooled anddiluted with diethyl ether. This solution was washed with H_2O and brine, dried (Na_2SO_4) and concentrated. The crude product was purified by column chromatography (silica, 15 to 25% ethyl acetate in hexanes) to give methyl cis and trans-(+/-)-6-(4-methoxyphenylsulfonyl)-4-phenylsulfanyl methyl-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate as a 2.5 to 1 mixture: MS: $(M+H)^+$ 504, $(M+NH_4)^+$ 521.

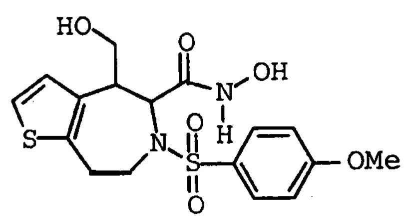
Step G: trans-(+/-)-6-(4-methoxyphenylsulfonyl)-4-phenylsulfanylmethyl-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylic acid

A mixture of methyl cis and trans-(+/-)-6-(4-methoxy phenylsulfonyl)-4-phenylsulfanylmethyl-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate was hydrolyzed with 1N LiOH as described above to give trans-(+/-)-6-(4-methoxyphenylsulfonyl)-4-phenylsulfanyl methyl-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylic acid as a single isomer: MS: $(M-H)^-$ 488.

Step H: trans-(+/-)-6-(4-methoxybenzenesulfonyl)-4-phenylsulfanylmethyl-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid

Trans-(+/-)-6-(4-methoxyphenylsulfonyl)-4-phenylsulfanyl methyl-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid was prepared from trans-(+/-)-6-(4-methoxyphenylsulfonyl)-4-phenylsulfanylmethyl-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylic acid in the same manner as trans-(+/-)-4-[2-(3,5-dimethyl phenyl)-ethyl]-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid: MS: $(M+H)^+$ 505, $(M+NH_4)^+$ 522.

Example 54



Preparation of trans-(+/-)-4-hydroxymethyl-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid

Step A: Methyl trans-(+/-)-4-(1,2-dihydroxyethyl)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate

Methyl trans-(+/-)-4-(1,2-dihydroxyethyl)-6-(4-methoxy phenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d] azepine-5-carboxylate, as a mixture of diastereomers, was prepared from methyl trans-(+/-)-6-(4-methoxyphenyl sulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4H-thieno[2,3-d] azepine-5-carboxylate in the same manner as cis-(+/-)-1-hydroxymethyl-6-(4-methoxyphenylsulfonyl)-1,3a,4,5,6,9b-hexahydro-2-oxa-7-thia-4-aza-cyclopenta[e]azulen-3-one. Diastereomer products, epimeric at the secondary alcohol center: MS (isomer 1): $(M+H)^+$ 442, $(M+NH_4)^+$ 459; MS (isomer 2): $(M+H)^+$ 442, $(M+NH_4)^+$ 459.

Step B: Methyl trans-(+/-)-4-formyl-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate

Methyl trans-(+/-)-4-formyl-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate was prepared from methyl trans-(+/-)-4-(1,2-dihydroxy ethyl)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate, a mixture of diastereomers, in the same manner as (+/-)-1-hydroxy-4-(4-methoxyphenylsulfonyl)-1,3a,4,5,6,9b-hexahydro-2-oxa-7-thia-4-aza-cyclopenta[e]azulen-3-one: ^1H NMR ($CDCl_3$,) δ 9.83 (s, 1H), 7.78 (d, 2H), 7.03 (d, 1H), 6.97 (d, 2H), 6.79 (d, 1H), 5.77 (d, 1H), 4.45 (d, 1H), 3.87 (s, 3H), 3.85 (m, 1H), 3.54 (s, 3H), 3.30 (m, 1H), 2.98 (m, 1H), 2.86 (m, 1H).

Step C: Methyl trans-(+/-)-4-hydroxymethyl-6-(4-methoxy phenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate

Methyl trans-(+/-)-4-hydroxymethyl-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate was prepared from methyl trans-(+/-)-4-formyl-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate in the same manner as cis-(+/-)-4-hydroxymethyl-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylic acid: MS: $(M+H)^+$ 412, $(M+NH_4)^+$ 429.

Step D: Methyl trans-(+/-)-4-(tert-butyldimethylsilanyl oxymethyl)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate

To a solution of methyl trans-(+/-)-4-hydroxymethyl-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate (36 mg, 0.088 mmol) in N,N-dimethylformamide (0.5 mL) at 0°C was added imidazole (7 mg, 0.1 mmol) and tert-butyldimethylsilyl

chloride (15 mg, 0.1 mmol). The reaction mixture was allowed to warm to 25°C and was stirred 6 hrs. This mixture was diluted with diethyl ether and washed with saturated aqueous potassium bisulfate, saturated aqueous sodium bicarbonate, and brine. The organic phase was dried (Na_2SO_4) and concentrated to give methyl trans-(+/-)-4-(tert-butyldimethylsilanyl oxymethyl)-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate: ^{1}H NMR ($CDCl_3$) δ 7.81 (d, 2H), 6.94 (d, 2H), 6.91 (d, 1H), 6.79 (d, 1H), 5.43 (d, 1H), 3.91 (dd, 1H), 3.87 (m, 1H), 3.86 (s, 3H), 3.75 (m, 1H), 3.68 (m, 1H), 3.51 (s, 3H), 3.26 (m, 1H), 3.03 (m, 1H), 2.78 (m, 1H), 0.90 (s, 9H), 0.05 (s, 3H), 0.01 (s, 3H).

<u>Step E: trans-(+/-)-4-(tert-butyldimethylsilanyloxy methyl)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylic acid</u>

Trans-(+/-)-4-(tert-butyldimethylsilanyloxymethyl)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylic acid was prepared from methyl trans-(+/-)-4-(tert-butyldimethylsilanyloxymethyl)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate in the same manner as trans-(+/-)-4-(2-(3,5-dimethylphenyl)ethyl)-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylic acid: MS: $(M+H)^+$ 512, $(M+NH_4)^+$ 529.

<u>Step F: trans-(+/-)-4-(tert-butyldimethylsilanyloxy methyl)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid</u>

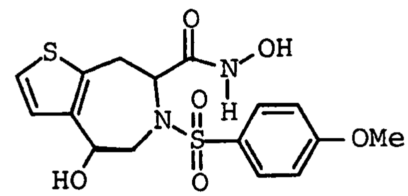
Trans-(+/-)-4-(tert-butyldimethylsilanyloxymethyl)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid was prepared from trans-(+/-)-4-(tert-butyldimethylsilanyloxymethyl)-6-(4-methoxy phenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno [2,3-d] azepine-5-carboxylic acid in the same manner as

trans-(+/-)-4-(2-(3,5-dimethylphenyl)ethyl)-6-(4-methoxy phenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d] azepine-5-hydroxamic acid: MS: $(M+H)^+$ 527, $(M+NH_4)^+$ 544.

Step G: trans-(+/-)-4-hydroxymethyl-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid

Trans-(+/-)-4-hydroxymethyl-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid was prepared from trans-(+/-)-4-(tert-butyldimethyl silanyloxymethyl)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid in the same manner as N-(2-{3-(3-hydroxypropenyl}thien-2-yl}ethyl)-N-(4-methoxyphenylsulfonyl)aminoacetic acid. The crude product was purified by trituration with diethyl ether to an off-white solid: MS: $(M-H)^-$ 411.

Example 55



Preparation of cis-(+/-)-4-Hydroxy-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-hydroxamic acid

Step A: Methyl 2-amino-3-thien-2-yl-propionate•HCl

3-(2-Thienyl)-DL-alanine (0.486 g, 2.84 mmoL) was suspended in methanol (4 mL) and hydrogen chloride gas was introduced into the mixture at 25°C until a clear solution formed. The solution was diluted with additional methanol (8 mL) and heated at reflux for 22 hrs. The solvent was removed under reduced pressure and the resulting residue was reconstituted in methanol and the solvent was again removed under reduced pressure. The white solid was purified by recrystallization from methanol-ether to give methyl 2-amino-3-thien-2-yl-propionate•HCl: ^{1}H NMR (D_2O, 400 MHz), ppm: 7.50 (d, 1H), 7.00 (d, 1H), 4.60 (d, 1H), 4.40(d, 1H). 4.38 (dd, 1H), 3.62 (dd, 1H), 3.39 (dd, 1H).

Step B: Methyl 2-(4-methoxyphenylsulfonylamino)-3-thien-2-yl-propionate

To a solution of methyl 2-amino-3-thiophen-2-yl-propionate•HCl (1 g, 4.51 mmoL) in N,N-dimethylformamide (10 mL) at 0°C was added diisopropylethylamine (1.7 mL, 9.8 mmoL), 4-methoxybenzenesulfonyl chloride (1.12 g, 5.4 mmoL) and a catalytic amount of 4-dimethylaminopyridine (55 mg, 0.45 mmoL). The reaction mixture was allowed to warm to 25°C and was stirred for 1.5 hrs. The mixture was then poured onto H_2O and ethyl acetate and separated. The organic phase was washed with saturated aqueous sodium bicarbonate, 1 M aqueous HCl, and brine, dried (Na_2SO_4), and concentrated to give

methyl 2-(4-methoxyphenylsulfonylamino)-3-thien-2-yl-propionate: MS: $(M+H)^+$ 356, $(M+NH_4)^+$ 373.

Step C: Methyl 2-(N-(tert-butoxycarbonylmethyl)-N-(4-methoxyphenylsulfonyl)amino)-3-thien-2-yl-propionate

To a solution of methyl 2-(4-methoxyphenylsulfonylamino)-3-thien-2-yl-propionate (1.82 g, 5.13 mmoL) in N,N-dimethylformamide (12 mL) was added tert-butyl bromoacetate (0.8 mL, 5.4 mmoL) and potassium carbonate (0.78 g, 5.6 mmoL). The reaction mixture was heated to 70°C for 1 hr and was then poured onto H_2O and ethyl acetate and separated. The organic phase was dried (Na_2SO_4) and concentrated to give methyl 2-(N-(tert-butoxycarbonylmethyl)-N-(4-methoxyphenylsulfonyl)amino)-3-thien-2-yl-propionate, which was carried to the next step without further purification: ^{1}H NMR ($CDCl_3$, 400 MHz), ppm: 7.82 (d, 2H), 7.10 (dd, 1H), 6.92 (d, 2H), 6.85 (dd, 1H), 6.77 (d, 1H), 4.55 (dd, 1H), 4.05 (ABq, 2H). 3.84 (s, 3H), 3.49 (s, 3H), 3.33 (dd, 1H), 3.15 (dd, 1H), 1.44 (s, 9H).

Step D: Methyl 2-(N-(carboxymethyl)-N-(4-methoxyphenyl sulfonyl)amino)-3-thien-2-yl-propionate

To a solution of crude methyl 2-(N-(tert-butoxycarbonyl methyl)-N-(4-methoxyphenylsulfonyl)amino)-3-thien-2-yl-propionate in methylene chloride (22 mL) at 0°C was added trifuoroacetic acid (7 mL). The reaction mixture was stirred for 1 hr at 0°C, concentrated and co-evaporated with toluene. The residue was purified by column chromatography (silica, 5 to 10% methanol in methylene chloride to give methyl 2-(N-(carboxymethyl)-N-(4-methoxyphenyl sulfonyl)amino)-3-thien-2-yl-propionate: ^{1}H NMR ($CDCl_3$, 400 MHz), ppm: 7.74 (d, 2H), 7.02 (d, 1H), 6.85 (d, 2H), 6.76 (bs, 1H), 6.69 (bs, 1H), 4.62 (m, 1H), 4.04 (m, 2H), 3.77 (s, 3H), 3.53 (s, 3H), 3.36 (m, 1H), 3.17 (m, 1H).

Step E: Methyl (+/-)-6-(4-methoxyphenylsulfonyl)-4-oxo-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-carboxylate

To a solution of methyl 2-(N-(carboxymethyl)-N-(4-methoxyphenyl sulfonyl)amino)-3-thien-2-yl-propionate (1.5 g, 3.63 mmoL) in methylene chloride (18 mL) at 0°C was added oxalyl chloride (0.4 mL, 4.59 mmoL), and a catalytic amount of N,N-dimethylformamide (0.1 mL). The reaction mixture was allowed to warm to 25°C over 1.5 hrs and was then cooled to -10°C and treated with a solution of tin(IV) tetrachloride (0.55 mL, 4.7 mmoL) in methylene chloride (5 mL). The reaction mixture was allowed to warm to -3°C over 2.5 hrs, diluted with methylene chloride and washed with 1N aqueous HCl. The organic layer was then dried ($MgSO_4$), concentrated, and purified by column chromatography (silica, 50% ethyl acetate in hexanes) to give methyl (+/-)-6-(4-methoxyphenyl sulfonyl)-4-oxo-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-carboxylate: MS: $(M+H)^+$ 396, $(M+NH_4)^+$ 413.

Step F: Methyl cis-(+/-)-4-hydroxy-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-carboxylate

Methyl cis-(+/-)-4-hydroxy-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-carboxylate was prepared from methyl (+/-)-6-(4-methoxyphenyl sulfonyl)-4-oxo-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-carboxylate in the same manner as cis-(+/-)-4-hydroxymethyl-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylic acid. The product was purified by column chromatography (silica, 2.5% methanol in methylene chloride): MS: $(M+H)^+$ 398, $(M+NH_4)^+$ 415.

Step G: cis-(+/-)-4-Hydroxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-carboxylic acid

Methyl cis-(+/-)-4-hydroxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-carboxylate was hydroyzed with aqueous LiOH as described above to give cis-(+/-)-4-Hydroxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-carboxylic acid: MS: $(M+H)^+$ 384, $(M+NH_4)^+$ 401.

Step H: 9-(4-methoxyphenylsulfonyl)-11-oxa-5-thia-9-aza-tricyclo[6.2.$20^{0,0}$]dodeca-2(6),3-dien-12-one

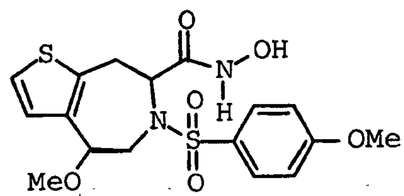
A solution of cis-(+/-)-4-Hydroxy-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-carboxylic acid (100 mg, 0.26 mmoL) in N,N-dimethyl formamide (5 mL) was treated with 1-hydroxybenzotriazole hydrate (40 mg, 0.3 mmoL). The solution was cooled to 0°C and treated with 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (55 mg, 0.29 mmoL). The reaction mixture was allowed to warm to 20°C and was stirred for 1.5 hrs. This mixture was diluted with ethyl acetate and washed with saturated aqueous $NaHCO_3$, 0.5 M aqueous HCl, and water. The organic phase was dried (Na_2SO_4) and concentrated to give the 9-(4-methoxyphenyl sulfonyl)-11-oxa-5-thia-9-aza-tricyclo[6.2.$20^{0,0}$]dodeca-2(6),3-dien-12-one: ^1H NMR ($CDCl_3$, 400 MHz), ppm: 7.75 (d, 2H), 7.17 (d, 1H), 6.98 (d, 2H), 6.81 (d, 1H), 5.38 (dd, 1H), 5.00 (dd, 1H), 3.90 (m, 1H), 3.86 (s, 3H), 3.57 (dd, 1H), 3.52 (dd, 1H), 3.41 (dd, 1H).

Step I: cis-(+/-)-4-Hydroxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-hydroxamic acid

cis-(+/-)-4-Hydroxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-hydroxamic acid was prepared from 9-(4-methoxyphenyl sulfonyl)-11-oxa-5-

thia-9-aza-tricyclo[6.2.20^{0,0}]dodeca-2(6),3-dien-12-one in the same manner as cis-(+/-)-4-[2-hydroxyethyl]-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid. The product was purified by column chromatography (silica, 2.5 to 5% methanol in methylene chloride): MS: $(M+H)^+$ 399, $(M+NH_4)^+$ 416.

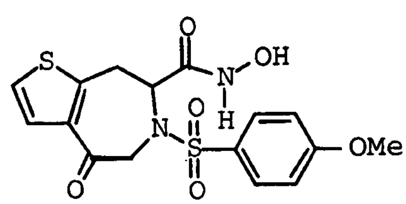
Example 56



Preparation of cis-(+/-)-4-methoxy-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-hydroxamic acid

cis-(+/-)-4-Methoxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-hydroxamic acid was prepared from methyl cis-(+/-)-4-hydroxy-6-(4-methoxy phenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d] azepine-7-carboxylate in the same manner as trans-(+/-)-6-(4-methoxyphenylsulfonyl)-4-(2-methoxyethyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid: MS $(M+H)^+$ 413.

Example 57

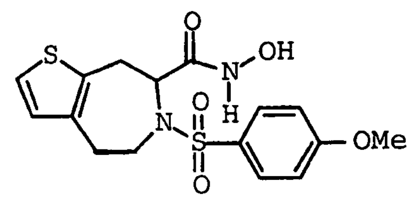


Preparation of (+/-)-6-(4-methoxyphenylsulfonyl)-4-oxo-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-hydroxamic acid

(+/-)-6-(4-Methoxyphenylsulfonyl)-4-oxo-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-hydroxamic acid was prepared from methyl (+/-)-6-(4-methoxyphenylsulfonyl)-4-oxo-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-

carboxylate in the same manner as trans-(+/-)-6-(4-methoxyphenylsulfonyl)-4-(2-methoxyethyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid: MS $(M+H)^+$ 397, $(M+NH_4)^+$ 414.

Example 58



Preparation of (+/-)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-hydroxamic acid

Step A: Methyl (+/-)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-carboxylate

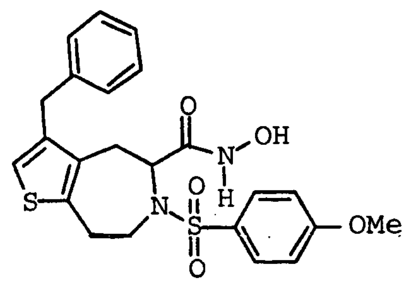
Methyl (+/-)-6-(4-methoxyphenylsulfonyl)-4-oxo-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-carboxylate (70 mg, 0.18 mmoL) was treated with trifluoroacetic acid (0.27 mL, 3.54 mmoL) and triethylsilane (0.085 mL, 0.531 mmoL) at 25°C. The reaction mixture was heated to 50°C for 45 minutes, cooled to 25°C, and then concentrated. The residue was co-evaporated with toluene (2X) and purified by column chromatography (silica, 25% ethyl acetate in hexanes) to give methyl (+/-)-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-carboxylate: ^1H NMR ($CDCl_3$, 400 MHz), ppm: 7.78 (d, 2H), 6.97 (d, 1H), 6.95 (d, 2H), 6.69 (d, 1H), 5.11 (dd, 1H), 3.95 (dt, 1H), 3.88 (s, 3H), 3.58 (s, 3H), 3.49 (dd, 1H), 3.45 (m, 1H), 3.30 (dd, 1H), 2.97 (m, 1H), 2.86 (m, 1H).

Step B: (+/-)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-hydroxamic acid

(+/-)-6-(4-Methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-hydroxamic acid was prepared from

methyl (+/-)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-carboxylate in the same manner as trans-(+/-)-6-(4-methoxyphenylsulfonyl)-4-(2-methoxyethyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid: MS $(M-H)^-$ 381.

Example 59



Preparation of (+/-)-3-benzyl-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-hydroxamic acid

Step A: Methyl (+/-)-3-(4-benzylthien-3-yl)-2-(N-(carboxymethyl)-N-(4-methoxyphenylsulfonyl)amino) propionate

Methyl (+/-)-3-(4-benzylthien-3-yl)-2-(N-(carboxymethyl)-N-(4-methoxyphenylsulfonyl)amino)propionate is prepared from methyl 3-(4-benzylthien-3-yl)-2-aminopropionate in the same manner as methyl 2-(N-(carboxymethyl)-N-(4-methoxyphenylsulfonyl)amino)-3-thiophen-2-yl-propionate: MS: $(M+H)^+$ 504, $(M+NH_4)^+$ 521.

Step B: Methyl (+/-)-3-benzyl-6-(4-methoxyphenyl sulfonyl)-8-oxo-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate and methyl (+/-)-3-benzyl-6-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-5-carboxylate

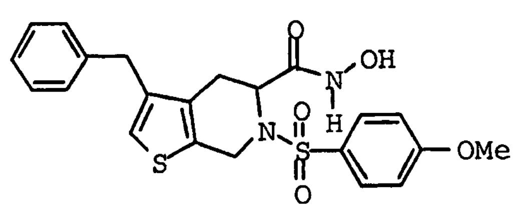
To a solution of methyl (+/-)-3-(4-benzylthien-3-yl)-2-(N-(carboxymethyl)-N-(4-methoxyphenylsulfonyl)amino) propionate (0.755 g, 1.5 mmoL) in toluene (9.5 mL) at

0°C was added oxalyl chloride (0.17 mL, 1.95 mmoL) and a catalytic amount of N,N-dimethylformamide (0.012 mL). The reaction mixture was allowed to warm to 25°C over 2 hrs and was then heated to reflux and treated with a tin(IV) tetrachloride (0.228 mL, 1.95 mmoL). The reaction mixture was heated for 20 minutes, poured onto ethyl acetate and 1N aqueous HCl and then separated. The organic layer was washed with brine, dried ($MgSO_4$), concentrated, and purified by column chromatography (silica, 0 to 1% methanol in methylene chloride) to give methyl (+/-)-3-benzyl-6-(4-methoxyphenyl sulfonyl)-8-oxo-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate: MS: $(M+H)^+$ 486, $(M+NH_4)^+$ 503; and methyl (+/-)-3-benzyl-6-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-5-carboxylate: MS: $(M+H)^+$ 458, $(M+NH_4)^+$ 475.

<u>Step C: (+/-)-3-benzyl-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-hydroxamic acid</u>

(+/-)-3-Benzyl-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-hydroxamic acid was prepared from methyl (+/-)-3-benzyl-6-(4-methoxyphenyl sulfonyl)-8-oxo-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate in the same manner as (+/-)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-hydroxamic acid: MS: $(M+H)^+$ 473, $(M+NH_4)^+$ 490.

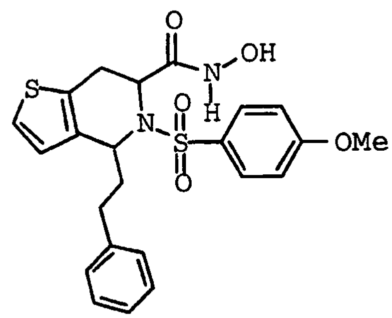
<u>Example 60</u>



Preparation of (+/-)-3-benzyl-6-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-5-hydroxamic acid

(+/-)-3-Benzyl-6-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-5-hydroxamic acid was prepared from methyl (+/-)-3-benzyl-6-(4-methoxyphenyl sulfonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-5-carboxylate in the same manner as trans-(+/-)-6-(4-methoxybenzenesulfonyl)-4-(2-methoxy-ethyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid: MS: $(M+H)^+$ 459, $(M+NH_4)^+$ 476.

Example 61



Preparation of cis- and trans-(+/-)-5-(4-methoxyphenyl sulfonyl)-4-phenethyl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-hydroxamic acid

Step A: Methyl (+/-)-2-(3-phenylpropionylamino)-3-thien-2-yl-propionate

A suspension of methyl 2-amino-3-thiophen-2-yl-propionate•HCl (3.5 g, 15.8 mmoL) in dichloromethane (25 mL) was treated with an aqueous (10 mL) solution of K_2CO_3 (4.6 g, 33.3 mmoL). This two phase mixture was cooled to 0°C and treated with a solution of hydrocinnamoyl chloride (2.6 mL, 17.5 mmoL) in dichloromethane (15 mL). The reaction mixture was allowed to warm to 25°C over 3 hrs. The mixture was diluted with dichloromethane and washed with water. The aqueous phase was re-extracted with dichloromethane and the combined ogranic phases were dried (Na_2SO_4) and concentrated. The white solid

was purified by recrystallization from ethyl acetate-ether to give methyl (+/-)-2-(3-phenylpropionylamino)-3-thien-2-yl-propionate: ^{1}H NMR ($CDCl_3$, 400 MHz), ppm: 7.15-7.35 (m, 6 H), 6.9 (m, 1 H), 6.6 (d, 1 H), 6.0 (d, 1 H), 4.9 (m, 1 H), 3.75 (s, 3 H), 3.35 (d, 2 H), 3.0 (m, 2 H), 2.55 (m, 2 H).

Step B: Methyl cis-(+/-)-4-phenethyl-6,7-dihydro-thieno[3,2-c]pyridine-6-carboxylate

A solution of methyl (+/-)-2-(3-phenylpropionylamino)-3-thien-2-yl-propionate (1.7 g, 5.4 mmoL) in acetonitrile (55 mL) was treated with $POCl_3$ (9 mL, 97 mmoL) and then heated at reflux for 6 hrs. The reaction mixture was concentrated under reduced pressure and then reconstituted in ethyl acetate. This solution was washed with saturated aqueous $NaHCO_3$ (2 times), water, and brine. The organic phase was then dried (Na_2SO_4) and concentrated to give methyl cis-(+/-)-4-phenethyl-6,7-dihydro-thieno[3,2-c]pyridine-6-carboxylate, which was carried onto the next step without purification.

Step C: Methyl cis-(+/-)-4-phenethyl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-carboxylate

A solution of methyl cis-(+/-)-4-phenethyl-6,7-dihydro-thieno[3,2-c]pyridine-6-carboxylate (0.222 g, 0.74 mmoL) in methanol (5 mL) was treated with PtO_2 (53 mg, 0.23 mmoL). The flask was evacuated and flushed with nitrogen (3X) and hydrogen (3X). The reaction mixture was then placed under an atmosphere of H_2 for 1 hr. The mixture was diluted with MeOH, filtered through a pad of celite, concentrated, and purified by flash chromatography (silica, 25% ethyl acetate in hexanes) to give methyl cis-(+/-)-4-phenethyl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-carboxylate: MS: $(M+H)^+$ 302, $(2M+H)^+$ 603.

Step D: cis-(+/-)-4-phenethyl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-carboxylic acid

A solution of methyl cis-(+/-)-4-phenethyl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-carboxylate (3.47 g, 11.5 mmoL) in methanol (30 mL) was cooled to 0°C and treated with 1N aqueous NaOH (11.8 mL). The reaction mixture was allowed to warm to 25°C and was stirred for 5 hrs. The methanol was removed under reduced pressure and the reaction mixture was diluted with water (100 mL) and acidified with 1N aqueous HCl (to pH 8). This solution was cooled to 0°C and the resulting solid was isolated by filtration to give cis-(+/-)-4-phenethyl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-carboxylic acid: MS: $(M+H)^+$ 288.

Step E: cis-(+/-)-5-(4-methoxyphenylsulfonyl)-4-phenethyl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-carboxylic acid

A suspension of cis-(+/-)-4-phenethyl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-carboxylic acid (3.14 g, 10.9 mmoL) in 9% aqueous Na_2CO_3 (13.6 mL, 11.6 mmoL) was cooled to 0°C and treated with a solution of 4-methoxybenzene sulfonyl chloride (3.12 g, 15.1 mmoL) in 1,4-dioxane (18 ml). The reaction mixture was allowed to warm to 25°C and was stirred for 5 hrs. The 1,4-dioxane was removed under reduced pressure and the reaction mixture was diluted with water and ethyl acetate. Filtration of the aqueous layer yielded recovered starting material. The aqueous filtrate was then treated with solid Na_2CO_3 (0.8 g) and was used to extract the original organic phase. The organic layer was again extracted with 1% aqueous Na_2CO_3 (2X) and the aqueous layers were combined and acidified with 1N aqueous HCl (to pH 2). The resulting suspension was extracted with ethyl acetate (2X), and the organic phases were combined, dried (Na_2SO_4), and concentrated to give cis-(+/-)-5-(4-methoxyphenyl sulfonyl)-4-phenethyl-

4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-carboxylic acid, which was carried onto the next step without purification: ^{1}H NMR ($CDCl_3$, 400 MHz), ppm: 7.66 (d, 2H), 7.1-7.3 (m, 5 H), 7.06 (d, 1 H), 6.86 (d, 2 H), 6.73 (d, 2 H), 5.16 (m, 1 H), 4.84 (dd, 1 H), 3.82 (s, 3H), 3.3 (dd, 1 H), 3.0 (m, 1 H), 2.8 (m, 1 H), 2.59 (dd, 1 H), 1.97 (m, 2 H).

Step F: cis and trans-(+/-)-5-(4-methoxyphenylsulfonyl)-4-phenethyl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-carboxylic acid benzhydryloxy-amide

A solution of cis- and trans-(+/-)-5-(4-methoxyphenyl sulfonyl)-4-phenethyl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-carboxylic acid (5:3)(300 mg, 0.656 mmoL) in N,N-dimethylformamide (8 mL) was treated with O-benzhydryl-hydroylamine (166 mg, 0.834 mmoL) and 1-hydroxybenzotriazole hydrate (116 mg, 0.858 mmoL). This solution was cooled to 0°C and treated with 1-(3-dimethylaminoprpyl)-3-ethylcarbodiimide hydrochloride (154 mg, 0.803 mmoL). The reaction mixture was allowed to warm to 25°C and was stirred for 8 hrs. This mixture was diluted with ethyl acetate and washed with saturated aqueous $NaHCO_3$, 0.5N aqueous HCl, water, and brine. The organic phase was dried (Na_2SO_4), concentrated, and purified by flash chromatography (silica, dichloromethane) to give the higher Rf cis-(+/-)-5-(4-methoxyphenylsulfonyl)-4-phenethyl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-carboxylic acid benzhydryloxy-amide and the lower Rf trans-(+/-)-5-(4-methoxyphenyl sulfonyl)-4-phenethyl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-carboxylic acid benzhydryloxy-amide: MS(cis): $(M+H)^+$ 639, $(M+NH_4)^+$ 656 and MS(trans): $(M+H)^+$ 639, $(M+NH_4)^+$ 656.

Step G: cis and trans-(+/-)-5-(4-methoxyphenylsulfonyl)-4-phenethyl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-hydroxamic acid

A solution of cis-(+/-)-5-(4-methoxyphenylsulfonyl)-4-phenethyl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-carboxylic acid benzhydryloxy-amide (228 mg, 0.357 mmoL) in dichloromethane (6 mL) was cooled to 0°C and treated with trifluoroacetic acid (6 mL), followed by dropwise treatment with triethylsilane (0.12 mL, 0.75 mmoL). The reaction mixture was allowed to warm to 25°C over 1 hr, concentrated and the residue was co-distilled with toluene. The crude reaction product was then purified by flash chromatography (silica, 5% methanol in dichloromethane) to give the higher Rf cis-(+/-)-5-(4-methoxyphenylsulfonyl)-4-phenethyl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-hyrdoxamic acid and the lower Rf trans-(+/-)-5-(4-methoxyphenylsulfonyl)-4-phenethyl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-hydroxamic acid: MS(cis): $(M+H)^+$ 473, $(M+NH_4)^+$ 490 and MS(trans): $(M+H)^+$ 473, $(M+NH_4)^+$ 490.

Example 62

Utilizing the procedures of Example 61, the compounds of Table II were prepared.

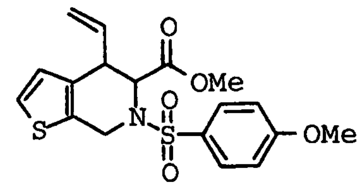
TABLE II

cis-(+/-)-5-(4-methoxyphenylsulfonyl)-4-methyl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-hydroxamic acid: MS $(M+H)^+$ 383, $(M+NH_4)^+$ 400.

trans-(+/-)-5-(4-methoxyphenylsulfonyl)-4-methyl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-hydroxamic acid: MS $(M+H)^+$ 383, $(M+NH_4)^+$ 400.

cis-(+/-)-4-benzyl-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-hydroxamic acid: MS $(M+H)^+$ 459, $(M+NH_4)^+$ 476.

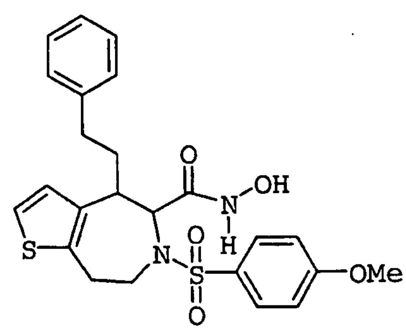
Example 63



Preparation of Methyl 6-(4-methoxyphenylsulfonyl)-4-vinyl-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-5-carboxylate

Methyl 6-(4-methoxyphenylsulfonyl)-4-vinyl-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-5-carboxylate was prepared from 3-bromo-2-(2-hydroxymethyl)thiophene and methyl (4-methoxyphenylsulfonylamino)acetate in the same manner as methyl cis-(+/-)-6-(4-methoxyphenylsulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-carboxylate was prepared: MS: $(M+NH4)^+$ 411.2.

Example 64



Preparation of trans-(+/-)-6-(4-methoxyphenylsulfonyl)-4-phenethyl-5,6,7,8-tetrahydro-4*H*-thieno[2,3-*d*]azepine-5-hydroxamic acid

Step A: Methyl (4-methoxyphenylsulfonylamino)acetate

Glycine methyl ester hydrochloride (20 g, 0.16 mol) was suspended in dichloromethane (320 mL), cooled to 0°C, and treated with diisopropylethylamine (69.4 mL, 0.4 mol). The resulting solution was allowed to stir for 15 minutes and was then treated with 4-methoxybenzene sulfonyl chloride (31 g, 0.15 mol) suspended in dichloromethane (165 mL). This reaction was allowed to

warm slowly to room temperature and stirred overnight. The reaction mixture was washed with 2 M aqueous HCl (3X), saturated aqueous $NaHCO_3$ (3X), and brine. The organic layer was dried ($MgSO_4$) and concentrated to yield sulfonamide as a white crystalline solid: R_f=0.09 (silica, 10% ethyl acetate in toluene); mp 60-62°C; MS (ESI, positive) m/z 260 (M+H), 277 ($M+NH_4$); HRMS (EI+) for $C_{10}H_{13}NO_5$ (M+), calcd 259.0514, found 259.0508; Anal. Calcd for $C_{10}H_{13}NO_5$: C, 46.33; H, 5.05; N, 5.40. Found: C, 46.32; H, 5.33, N, 5.44.

Step B: Methyl N-(2-(3-bromothiophen-2-yl)ethyl)-N-(4-methoxyphenylsulfonyl)aminoacetate

A solution of triphenylphosphine (12.3 g, 46.9 mmol) in THF (400 mL) was cooled to 0°C and treated with diisopropylazodicarboxylate (9.2 mL, 46.8 mmol). To this was added 2-(3-bromothiophen-2-yl)ethanol (Keegstra et al., Tetrahedron 48:3633-3652 (1992)) (9.65 g, 46.6 mmol), followed by methyl (4-methoxyphenylsulfonylamino) acetate (15.1 g, 58.3 mmol). The resulting solution was warmed to ambient temperature and stirred for 24 h. TLC (silica, 10% ethyl acetate in toluene) indicated starting materials remained so additional quantities of triphenylphosphine (5.9 g, 22.5 mmol) and diisopropyl azodicarboxylate (4.1 mL, 20.8 mmol) were added and the mixture was stirred another 1 h. The solvents were evaporated and the residue was purified by column chromatography (silica 5% ethyl acetate in toluene) followed by trituration with 5% ethyl acetate in hexanes to give the desired product as a white solid. This product could be recrystallized from ethyl acetate-hexanes; R_f=0.4 (silica, 10% ethyl acetate in toluene); mp 79-80°C (ethyl acetate-hexanes); MS (ESI, positive) m/z 448 (M+H, ^{79}BR), 450 (M+H, ^{81}Br), 465 ($M+NH_4$, ^{79}Br), 467 ($M+NH_4$, ^{81}Br); HRMS (FAB) for $C_{16}H_{19}NO_5S_2Br$ (M+H, ^{79}Br), calcd 447.9915; Anal. Calcd for $C_{16}H_{18}NO_5S_2Br$: C, 42.86; H, 4.05; N, 3.12. Found: C, 42.88; H, 3.94; N, 3.10.

Step C: Methyl N-(2-(3-(3-(*tert*-butyldimethylsilanyl oxy)propenyl)thiophen-2-yl)ethyl)-N-(4-methoxyphenyl sulfonyl)aminoacetate

Methyl N-(2-(3-bromothiophen-2-yl)ethyl)-N-(4-methoxy phenylsulfonyl)aminoacetate (2.38 g, 5.3 mmol) was dissolved in toluene (35 mL) and treated with (Z)-$^{n}Bu_3SnCHCHCH_2OSi^{t}BuMe_2$ (Jung et al., Tet. Lett. 23:3851-3854 (1982)). This solution was heated to reflux for 5 minutes and then treated with dichlorobis(triphenyl phosphine)palladium (II) (289 mg, 0.4 mmol). The reaction mixture was stirred at reflux for 1.5 h and then cooled to 0°C. The mixture was diluted with diethyl ether and stirred vigorously with 10% aqueous potassium fluoride for 1 hr. Filtration through a plug of celite removed the solid by-products. The liquid phases of the filtrate were separated and the organic layer was washed with 10% aqueous potassium fluoride, dried (Na_2SO_4) and concentrated. The tan oil was purified by flash chromatography (silica, 10 to 15% ethyl acetate in hexanes) to give the desired product as a yellow oil: R_f=0.25 (silica, 25% ethyl acetate in hexanes); MS (ESI, positive) m/z 557 ($M+NH_4$); Anal. Calcd for $C_{25}H_{37}NO_6S_2Si$: C, 55.63; H, 6.91; N, 2.59. Found: C, 55.52; H, 6.94; N, 2.46.

Step D: N-(2-(3-(3-Hydroxypropenyl)thiophen-2-yl) ethyl)-N-(4-methoxyphenylsulfonyl)aminoacetic acid

To a stirred solution of methyl N-(2-(3-(3-(*tert*-butyldimethylsilanyloxy)propenyl)thiophen-2-yl)ethyl)-N-(4-methoxyphenylsulfonyl)aminoacetate (4.33 g, 8 mmol) dissolved in THF (8mL) at 0°C was added 1 M aqueous KOH (12 mL). The reaction mixture was allowed to warm to 25°C and was stirred for 3 h. The THF was removed under reduced pressure and the reaction mixture was diluted with water and acidified with 1 N HCl (12 mL). The white precipitate was extracted into ethyl acetate (2X)

and the combined organic layers were dried (Na_2SO_4) and concentrated to give crude N-(2-(3-(3-(*tert*-butyl dimethylsilanyloxy)propenyl)thiophen-2-yl)ethyl)-N-(4-methoxyphenylsulfonyl)aminoacetic acid (4.4 g), which was carried onto the next step without purification: R_f=0.6 (silica, 10% methanol in dichloromethane with 1% acetic acid); MS (ESI, positive) m/z 543 ($M+NH_4$); MS (ESI, negative) m/z 524 (M-H). To a stirred solution of the crude carboxylic acid dissolved in THF (70mL) at 0°C was added a 1 M solution of TBAF in THF (16 mL, 16 mmol). The reaction mixture was allowed to warm to 25°C and was stirred for 5 h. The THF was removed under reduced pressure and the residue was redissolved in ethyl acetate. This solution was washed with 1 N HCl, water and brine. The organic phase was then dried (Na_2SO_4) and concentrated to give a tan oil, which solidified upon trituration with diethyl ether. The solid product was collected on a buchner funnel and rinsed with cold diethyl ether to give the desired product as a light tan solid in a 20 to 1 ratio of cis to trans isomers. Data for the major (cis) isomer: R_f=0.37 (silica, 10% methanol in dichloromethane with 1% acetic acid); mp 109.5-115°C (ethyl acetate-hexanes); MS (ESI, positive) m/z 394 ($M-H_2O+H$), 429 ($M+NH_4$); MS (ESI, negative) m/z 410 (M-H); HRMS (FAB-) for $C_{18}H_{20}NO_6S_2$ (M-H), calcd 410.0732, found 410.0718; Anal. Calcd for $C_{18}H_{21}NO_6S_2$: C, 52.24; H, 5.14; N, 3.40. Found: C, 52.25; H, 4.83; N, 3.33.

<u>Step E: 10-(4-Methoxyphenylsulfonyl)-9,10,11,12-tetrahydro-6H-7-oxa-1-thia-10-aza-cyclopenta cycloundecen-8-one</u>

A solution of N-(2-(3-(3-hydroxypropenyl)thiophen-2-yl) ethyl)-N-(4-methoxyphenylsulfonyl)aminoacetic acid, a 20:1 mixture of cis to trans isomers (1.45 g, 3.5 mmol) dissolved in acetonitrile (25 mL) was treated with triethylamine (3.9 mL, 28.1 mmol). This solution was

slowly added (15 hrs, via syringe pump) to a solution of 2-chloro-1-methylpyridinium iodide (3.6 g, 14.1 mmol) in acetonitrile (500 mL) heated at reflux. The reaction mixture was heated another 5 hrs at reflux and then the acetonitrile was evaporated. The residue was suspended in ethyl acetate and the solid by-products were removed via filtration. The filtrate was concentrated and the crude product was purified by flash chromatography (silica, 25 to 40% ethyl acetate in hexanes) to give the desired product as a white solid. This product could be recrystallized from ethyl acetate-hexanes: R_f=0.43 (silica, 50% ethyl acetate in hexanes); mp 138.5-140°C (ethyl acetate-hexanes); MS (ESI, positive) m/z 394 (M+H), 411 (M+NH_4); HRMS (EI+) for $C_{18}H_{19}NO_5S_2$ (M+), calcd 393.0705, found 393.0701; Anal. Calcd for $C_{18}H_{19}NO_5S_2$: C, 54.94; H, 4.87; N, 3.56. Found: C, 54.93; H, 4.85; N, 3.56.

Step F: Methyl cis-(+/-)-6-(4-methoxyphenylsulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4*H*-thieno[2,3-*d*]azepine-5-carboxylate

To a solution of 10-(4-methoxyphenylsulfonyl)-9,10,11,12-tetrahydro-6H-7-oxa-1-thia-10-aza-cyclopenta cycloundecen-8-one (1.31 g, 3.3 mmol) dissolved in THF (33 mL) at -78°C was added TBSOTf (0.8 mL, 3.5 mmol) followed immediately by a 0.5 M solution of KHMDS in toluene (7 mL, 3.5 mmol). The cooling bath was then removed and the reaction mixture was allowed to warm to 25°C, over 30 minutes. The mixture was then heated to reflux for 4 hrs. The mixture was cooled to 25°C and poured onto a mixture of ethyl acetate and saturated aqueous NH_4Cl. The layers were separated and the organic phase was washed with H_2O and brine, dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography (silica, 25 to 50% ethyl acetate in hexanes followed by 5 to 10% methanol in methylene

chloride) to give *tert*-butyldimethylsilyl cis-(+/-)-6-(4-methoxyphenylsulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4*H*-thieno[2,3-*d*]azepine-5-carboxylate as a clear oil: R_f=0.66 (silica, 50% ethyl acetate in hexanes, decomposed on silica gel plate); ^{1}H NMR (400 MHz, $CDCl_3$) δ7.74 (m, 2H), 6.95-6.90 (m, 3H), 6.81 (d,J=5.0 Hz 1H), 6.47 (m, 1H), 5.27 (d,J=10 Hz, 1H, 5.23 (d,J=17.5 Hz, 1H), 4.90 (d,J=3 Hz, 1H), 4.02-3.95 (m, 2H), 3.85 (s, 3H), 3.55 (m, 1H), 3.13 (m, 1H), 2.94 (m, 1H), 0.84 (s, 9H), 0.07 (s, 3H), 0.04 (s, 3H); ^{1}H NMR (400 MHz, THF-d_8) δ7.73 (m, 2H), 7.00 (m, 2H), 6.99 (d, 1H), 6.80 (d,J=5 Hz, 1H), 6.55 (ddd,J=17.0, 10.0, 9.0 Hz, 1H), 5.22 (d,J=10 Hz, 1H), 5.21 (dd,J=17.0, 1.0 Hz, 1H), 4.93 (d,J=2.5 Hz, 1H), 3.97-3.91 (m, 2H), 3.83 (s, 3H), 3.51 (m, 1H), 3.06 (m, 1H), 2.93 (m, 1H), 0.85 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H); and cis-(+/-)-6-(4-methoxyphenylsulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4*H*-thieno[2,3-*d*]azepine-5-carboxylic acid, as a tan foam: R_f=0.35 (silica, 10% methanol in dichloromethane); MS (ESI, positive) m/z 394 (M+H), 411 ($M+NH_4$). To a solution of *tert*-butyldimethylsilyl cis-(+/-)-6-(4-methoxyphenylsulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4*H*-thieno[2,3-*d*]azepine-5-carboxylate (72 mg, 0.14 mmol) dissolved in methanol and THF (3:1, 2.4 mL) at 0°C was added a solution of K_2CO_3 (60 mg, 0.43 mmol) in H_2O (.6 mL). This cloudy reaction mixture was allowed to warm to 25°C, over 30 minutes, and was then concentrated to 1/4th of the original volume. Dilution with H_2O and acidification with 1 N HCl (to pH 2) gave a white precipitate that was extracted into ethyl acetate. The organic phase was dried (Na_2SO_4) and concentrated to give the additional cis-(+/-)-6-(4-methoxyphenylsulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4*H*-thieno[2,3-*d*]azepine-5-carboxylic acid, which was carried to the next step without further purification. To a solution of the carboxylic acid (323 mg, 0.82 mmol) dissolved in benzene

and methanol (2:1, 9 mL) at 0°C was added a 2 M solution of $TMSCHN_2$ in hexanes (0.82 mL, 1.64 mmol). The reaction mixture was stirred 15 minutes and then the solvents were removed under reduced pressure. The residue was purified by flash chromatography (silica, 25 to 38% ethyl acetate in hexanes followed by 5 to 10% methanol in methylene chloride) to give the desired product as a white solid: R_f=0.47 (silica, 50% ethyl acetate in hexanes) and R_f=0.51 (silica, 10% ethyl acetate in toluene); mp 112-113°C; MS (ESI, positive) m/z 408 (M+H), 425 ($M+NH_4$); HRMS (EI+) for $C_{19}H_{21}NO_5S_2$ (M+), calcd 407.0861, found 407.0848; Anal. Calcd for $C_{19}H_{21}NO_5S_2$: C, 56.00; H, 5.19; N, 3.44. Found: C, 56.15; H, 4.88; N, 3.34.

Step G: Methyl cis-(+/-)-6-(4-methoxyphenylsulfonyl)-4-phenethyl-5,6,7,8-tetrahydro-4*H*-thieno[2,3-*d*]azepine-5-carboxylate

To a solution of methyl cis-(+/-)-6-(4-methoxyphenyl sulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4*H*-thieno[2,3-*d*]azepine-5-carboxylate (77 mg, 0.19 mmol) dissolved in THF (3 mL) at 0°C was added a 0.5 M solution of 9-BBN in THF (0.625 mL, 0.31 mmol). The reaction mixture was allowed to warm to 25°C, over 3.5 hrs, and was then treated sequentially with $PdCl_2(dppf)\bullet CH_2Cl_2$ (18 mg, 0.02 mmol), iodobenzene (0.17 mL, 1.5 mmol), K_2CO_3 (108 mg, 0.78 mmol), DMF (1 mL), and H_2O (0.15 mL). After stirring 1 h at 25°C the solution was diluted with diethyl ether and washed with H_2O, 1 N HCl, saturated aqueous $NaHCO_3$, 10% aqueous Na_2SO_3, and brine. The organic layer was dried (Na_2SO_4), concentrated, and purified by column chromatography (silica, 3% ethyl acetate in toluene) to give the desired product as a white foam: R_f=0.47 (silica, 10% ethyl acetate in toluene); MS (ESI, positive) m/z 486 (M+H), 503 ($M+NH_4$); HRMS (EI+) for $C_{25}H_{27}NO_5S_2$ (M+), calcd 485.1331, found 485.1282.

Step H: trans-(+/-)-6-(4-Methoxyphenylsulfonyl)-4-phenethyl-5,6,7,8-tetrahydro-4*H*-thieno[2,3-*d*]azepine-5-carboxylic acid

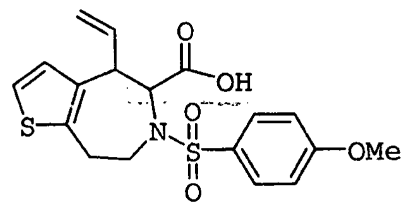
To a solution of methyl cis-(+/-)-6-(4-methoxyphenyl sulfonyl)-4-phenethyl-5,6,7,8-tetrahydro-4*H*-thieno[2,3-*d*]azepine-5-carboxylate (95 mg, 0.2 mmol) dissolved in THF and H_2O (3:1, 4 mL) was added 1 M aqueous LiOH (0.6 mL, 0.6 mmol). The reaction mixture was heated to reflux for 18 h and then the THF was removed *in vacuo*. Dilution with H_2O followed by acidification with 2 N HCl (to pH 2) gave a white precipitate that was extracted into ethyl acetate. The organic layer was then dried (Na_2SO_4), concentrated, and purified by column chromatography (silica, 5 to 10% methanol in dichloromethane) to give the desired product as a white foam: R_f=0.5 (silica, 10% methanol in dichloromethane); mp 177-178°C ($CHCl_3$); MS (ESI, positive) m/z 489 ($M+NH_4$); MS (ESI, negative) m/z 470 (M-H); HRMS (FAB+) for $C_{24}H_{26}NO_5S_2$ (M+H), calcd 472.1252, found 472.1262.

Step I: trans-(+/-)-6-(4-Methoxyphenylsulfonyl)-4-phenethyl-5,6,7,8-tetrahydro-4*H*-thieno[2,3-*d*]azepine-5-hydroxamic acid

A solution of trans-(+/-)-6-(4-methoxyphenylsulfonyl)-4-phenethyl-5,6,7,8-tetrahydro-4*H*-thieno[2,3-*d*]azepine-5-carboxylic acid (48 mg, 0.1 mmol) dissolved in CH_2Cl_2 (5 mL) at 0°C was treated sequentially with hydroxylamine hydrochloride (28 mg, 0.4 mmol), diisopropylethylamine (90 µL, 0.52 mmol), and PyBroP (59 mg, 0.13 mmol). This mixture was allowed to warm to 25°C over 1.5 hrs and was then concentrated. The residue was dissolved in ethyl acetate and the remaining solids were removed via filtration. The filtrate was washed with brine, 1 N HCl, and brine again. The organic phase was then dried (Na_2SO_4), concentrated, and purified by column chromatography (silica, 2.5% methanol in methylene

chloride) to give the desired product as a white foam. This product could be recrystallized from diethyl ether-hexanes: R_f=0.5 (silica, 7.5% methanol in dichloromethane); MS (ESI, positive) m/z 504 ($M+NH_4$); MS (ESI, negative) m/z 485 (M-H); HRMS (FAB+) for $C_{24}H_{27}N_2O_5S_2$ (M+H), calcd 487.1361, found 487.1381; Anal. Calcd for $C_{24}H_{26}N_2O_5S_2$: C, 59.24; N, 5.76. Found: C, 59.46; H, 5.34; N, 5.58.

Example 65

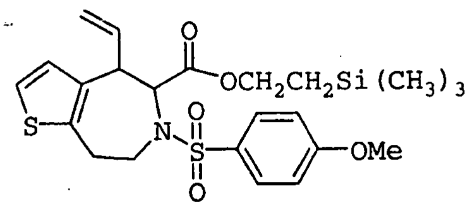


Preparation of trans-(+/-)-6-(4-Methoxyphenylsulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4H-thieno[2,3-*d*]azepine-5-carboxylic acid and its methyl ester

To a solution of the methyl cis-(+/-)-6-(4-methoxyphenylsulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4*H*-thieno[2,3-*d*]azepine-5-carboxylate (365 mg, 0.9 mmol) dissolved in THF and H_2O (3:1, 16 mL) at ambient temperature was added a 1 M aqueous solution of LiOH (2.7 mL, 2.7 mmol). This solution was heated to reflux for 18 h and then cooled to room temperature. The THF was removed in vacuo and the resulting aqueous solution was diluted with H_2O and acidified with 2 N HCl (to pH2). The cloudy mixture was extracted into ethyl acetate (2X) and the combined organic layers were dried (Na_2SO_4), filtered and concentrated to give the desired product as a tan solid: R_f=0.35 (silica, 10% methanol in dichloromethane); MS (ESI, negative) m/z 392 (M-H). To confirm that the base had indeed induced epimerization, the methyl ester of the trans carboxylic acid was prepared. To a solution of trans carboxylic acid (280 mg, 0.71 mmol) dissolved in benzene and methanol (2:1, 10.5 mL) at 0°C was added a 2 M solution

of $TMSCHN_2$ (1.05 mL, 2.1 mmol) in hexanes. The reaction mixture was stirred 15 minutes and then the solvents were removed under reduced pressure. The residue was purified by flash chromatography (silica, 0.5% methanol in methylene chloride) to give the trans methyl ester as a white foam: R_f=0.68 (silica, 75% ethyl acetate in hexanes) and R_f=0.46 (silica, 10% ethyl acetate in toluene; MS (ESI, positive) m/z 408 (M+H), 425 ($M+NH_4$); HRMS (EI+) for $C_{19}H_{21}NO_5S_2$ (M+), calcd 407.0861, found 407.0881.

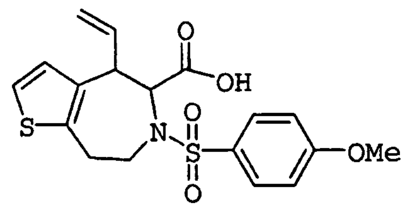
Example 66



Preparation of 2-(trimethylsilyl)ethyl cis-(+/-)-6-(4-methoxyphenylsulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4*H*-thieno[2,3-*d*]azepine-5-carboxylate

A solution of cis-(+/-)-6-(4-methoxyphenylsulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4*H*-thieno[2,3-*d*]azepine-5-carboxylic acid (33 mg, 0.08 mmol) in CH_2Cl_2 (1 mL) was treated with a catalytic amount of DMAP followed by the 2-(trimethylsilyl)ethanol (12 mL, 0.08 mmol). This solution was then cooled to 0ºC and treated with DCC (17 mg, 0.08 mmol). The reaction mixture was stirred 1 h at 0ºC and then poured onto a mixture of CH_2Cl_2 and 0.1 N HCl. The aqueous layer was extracted with additional CH_2Cl_2 and the combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated. The residue was purified by column chromatography (silica, 15% ethyl acetate in hexanes) to give the desired product as a clear oil in a 10 to 1 ratio of cis to trans isomers. Data for the major cis isomer: R_f=0.78 (silica, 5% methanol in dichloromethane); MS (ESI, positive) m/z 494 (M+H), 511 ($M+NH_4$).

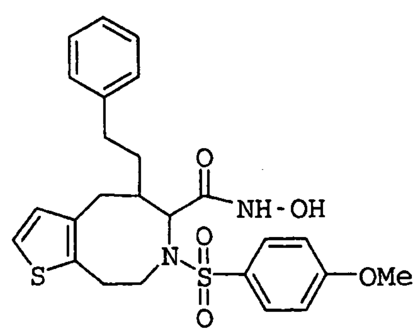
Example 67



Preparation of cis-(+/-)-6-(4-methoxyphenylsulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4*H*-thieno[2,3-*d*]azepine-5-carboxylic acid

To a solution of 2-(trimethylsilyl)ethyl cis-(+/-)-6-(4-methoxyphenylsulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4*H*-thieno[2,3-*d*]azepine-5-carboxylate (7 mg; 10:1 mixture of cis and trans isomers) dissolved in THF (0.75 mL), cooled to 0°C, was added a 1 M solution of TBAF in THF (20 µL). This solution was stirred for 20 minutes and then concentrated. The residue was dissolved in EtOAc and washed with 0.1 N HCl. The aqueous layer was back extracted with EtOAc and the combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated to give the desired carboxylic acid. The ^{1}H NMR indicated a 10:1 mixture of cis and trans isomers, with the major compound NMR matching that of the previously prepared carboxylic acid.

Example 68



Preparation of trans-(+/-)-7-(4-methoxyphenylsulfonyl)-5-phenethyl-4,5,6,7,8,9-hexahydrothieno[2,3-*d*]azocine-6-hydroxamic acid

Step A: Methyl N-(4-methoxyphenylsulfonyl)-N-(2-(3-vinylthiophen-2-yl)ethyl)aminoacetate

A solution of methyl N-(2-(3-bromothiophen-2-yl)ethyl)-N-(4-methoxyphenylsulfonyl)aminoacetate (5.5 g, 12.3 mmol) in toluene (75 mL) was treated with tributylvinyltin (9 mL, 30.8 mmol) and then heated to reflux. The hot solution was treated with dichloro bis(triphenylphosphine)palladium(II) (625 mg, 0.89 mmol) and stirred at reflux for 24 h. Proton NMR analysis of the reaction mixture indicated starting material remained so an additional quantity of dichloro bis(triphenylphosphine)palladium(II) (600 mg, 0.85 mmol) was added and the mixture was stirred another 7 h at reflux. After cooling to ambient temperature, the mixture was diluted with diethyl ether and stirred vigorously with 10% aqueous potassium fluoride for 1 hr. Filtration through a plug of celite removed the solid by-products. The liquid phases of the filtrate were separated and the organic layer was washed with 10% aqueous potassium fluoride, dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography (silica, 25 to 40% ethyl acetate in hexanes) to give the desired product as a yellow solid: R_f = 0.45 (silica, 50% ethyl acetate in hexanes); mp 69-72 °C; MS (ESI, positive) m/z 396 (M+H), 413 ($M+NH_4$); HRMS (FAB+) for $C_{18}H_{21}NO_5S_2$(M+H), calcd 396.0939, found 396.0950; Anal. Calcd for $C_{18}H_{21}NO_5S_2$: C, 54.66; H, 5.35; N, 3.54. Found: C, 54.85; H, 5.31; N, 3.43.

Step B: Methyl N-(2-(3-formylthiophen-2-yl)-ethyl)-N-(4-methoxyphenylsulfonyl)aminoacetate

To a solution of methyl N-(4-methoxyphenylsulfonyl)-N-(2-(3-vinylthiophen-2-yl)ethyl)aminoacetate (3.25 g, 8.2 mmol) dissolved in THF and H_2O (4:1, 85 ml) was added to a 2.5 wt.% solution of osmium tetroxide in 2-methyl-2-propanol (4.1 ml, 0.33 mmol) and sodium metaperiodate (2.2 g, 10.3 mmol). The mixture was then treated with a

second portion of sodium metaperiodate (2.2 g, 10.3 mmol) and stirred for 1 h, at 25°C. The THF was then evaporated and the mixture was diluted with H_2O and the product was extracted into ethyl acetate (2X). The combined organic layers were washed with brine, dried ($MgSO_4$), concentrated and purified by column chromatography (silica, 25 to 50% ethyl acetate in hexanes) to give the desired product as a light tan solid: R_f = 0.3 (silica, 50% ethyl acetate in hexanes); mp 79-81°C; MS (ESI, positive) m/z 398 (M+H), 415 ($M+NH_4$); HRMS (FAB+) for $C_{17}H_{20}NO_6S_2$ (M+H), calcd 398.0732, found 398.0747; Anal. Calcd for $C_{17}H_{19}NO_6S_2$: C, 51.37; H, 4.82; N, 3.52. Found: C, 51.36; H, 4.48; N, 3.50.

<u>Step C: Methyl N-(2-(3-(hydroxymethyl)thiophen-2-yl)-ethyl)-N-(4-methoxyphenylsulfonyl)aminoacetate</u>

To a solution of methyl N-(2-(3-formylthiophen-2-yl)-ethyl)-N-(4-methoxyphenylsulfonyl)aminoacetate (1.43 g, 3.6 mmol) dissolved in methanol and dichloromethane (3:1) 36 ml) was added the $NaBH_4$ (138 mg, 3.65 mmol). The mixture was stirred at ambient temperature for 30 minutes and then concentrated in vacuo. The residue was dissolved in dichloromethane and washed with 1 N HCl and H_2O. The organic layer was dried (Na_2SO_4), concentrated, and purified by column chromatography (silica, 50 to 75% ethyl acetate in hexanes) to give the desired product as a white solid: R_f = 4.6 (silica, 75% ethyl acetate in hexanes); mp 83-85 °C; MS (ESI, positive) m/z 382 ($M+H-H_2O$), 417 ($M+NH_4$); HRMS (FAB+) for $C_{17}H_{20}NO_5S_2$ ($M+H-H_2O$), calcd 382.0783, found 382.0814; Anal. Calcd f$_1$or $C_{17}H_{21}NO_6S_2$: C, 51.11; H, 5.30; N, 3.51. Found: C, 50.95; H, 5.20; N, 3.46.

<u>Step D: Methyl N-(2-(3-(bromomethyl)thiophen-2-yl)-ethyl)-N-(4-methoxyphenylsulfonyl)aminoacetate</u>

To a solution of methyl N-(2-(3-(hydroxymethyl)thiophen-2-yl)-ethyl)-N-(4-methoxyphenylsulfonyl)aminoacetate

(0.97 g, 2.43 mmol) dissolved in dichloromethane (21 ml), cooled to -30ºC, was added PPh_3 (795 mg, 3 mmol) and recrystallized NBS (550 mg, 3.1 mmol). This solution was stirred for 30 minutes, diluted with diethyl ether, and then washed with saturated aqueous sodium carbonate. Addition of H_2O was required to dissolve solids that had formed during the wash. The organic layer was washed with a 1% solution of Na_2SO_3 (93 ml) and brine, dried (Na_2SO_4, concentrated, and purified by column chromatography (silica, 25 to 38% ethyl acetate in hexanes) to give the desired product as a white solid. This product could be recrystallized from ethyl acetate-hexanes: R_f = 0.63 (silica, 75% ethyl acetate in hexanes); mp 73-74ºC (ethyl acetate in hexanes); Anal. Calcd f,or $C_{17}H_{20}NO_5S_2Br$: C, 44.16; H, 4.36; N, 3.03. Found: C, 44.05; H, 4.30; N, 2.98.

Step E: Methyl N-(2-(3-(4-(*tert*-butyldimethyl silanyloxy)but-2-enyl)thiophen-2-yl)ethyl)-N-(4-methoxyphenylsulfonyl)aminoacetate

Methyl N-(2-(3-(4-(*tert*-butyldimethylsilanyloxy)but-2-enyl)thiophen-2-yl)ethyl)-N-(4-methoxyphenylsulfonyl) aminoacetate was prepared from methyl N-(2-(3-(bromo methyl)thiophen-2-yl)-ethyl)-N-(4-methoxyphenylsulfonyl) aminoacetate (1.26 g, 2.7 mmol) according to the same procedure used for the preparation of methyl N-(2-(3-(3-(*tert*-butyldimethyl silanyloxy)propenyl)thiophen-2-yl)ethyl)-N-(4-methoxy phenylsulfonyl)aminoacetate, using (Z)$^nBu_3SnCH{=}CHCH_2OSi^tBuMe_2$ (20:1; Z:E), and $PdCl_2(PPh_3)_2$ (150 mg, 0.21 mmol) in toluene (30 ml). The residue was purified by flash chromatography (silica, 25% ethyl acetate in hexanes) to give the desired product as a tan oil in a 20:1 ratio of cis to trans isomers. Data for the major (cis) isomer: R_f = 0.28 (silica, 50% ethyl acetate in hexanes); MS (ESI, positive) m/z 554 (M+H), 571 ($M+NH_4$); HRMS (FAB+) for $C_{26}H_{40}NO_6S_2Si$ (M+H), calcd 554.2066, found 554.2051; Anal.

Calcd for $C_{26}H_{39}NO_6S_2Si$: C, 56.39; H, 7.10; N, 2.53. Found: C, 56.60; H, 7.06; N, 2.33.

Step F: N-(2-(3-(3-Hydroxybut-2-enyl)thiophen-2-yl) ethyl)-N-(4-methoxyphenylsulfonyl)aminoacetic acid

N-(2-(3-(3-Hydroxybut-2-enyl)thiophen-2-yl)ethyl)-N-(4-methoxyphenylsulfonyl)aminoacetic acid was prepared from methyl N-(2-(3-(4-(*tert*-butyldimethylsilanyloxy)but-2-enyl)thiophen-2-yl)ethyl)-N-(4-methoxyphenylsulfonyl) aminoacetate (20:1 (Z:E) mixture, 1.07 g, 1.93 mmol) according to the same procedure used for the preparation of N-(2-(3-(3-Hydroxypropenyl)thiophen-2-yl) ethyl)-N-(4-methoxyphenylsulfonyl)aminoacetic acid, using 1 N KOH (3 ml) dissolved in THF (20ml). The N-(2-(3-(4-(*tert*-butyldimethylsilanyloxy)but-2-enyl)thiophen-2-yl)ethyl)-N-(4-methoxyphenylsulfonyl)aminoacetic acid intermediate (1.05 g) (R_f = 0.6 (silica, 10% methanol in dichloromethane with 1% acetic acid); MS (ESI, negative) m/z 424 (M-Si^{t}BuMe$_2$), 538 (M-H); HRMS (FAB+) for $C_{27}H_{38}NO_6S_2Si$ (M+H), calcd 540.1910, found 540.1885) was treated with a 1 M solution of TBAF in THAF in THF (3.7 ml) dissolved in THF (20 ml). After trituration with ether and recrystallization of the filtrates from dichloromethane-hexanes, the desired product was obtained as a tan solid in a 10 to 1 ratio of cis to trans isomers. Data for the major (cis) isomer: R_f = 0.34 (silica, 10% methanol in dichloromethane with 1% acetic acid); mp 109-110.5°C (dichloromethane-hexanes); MS (ESI, positive) m/z 443 (M+NH$_4$); MS (ESI, negative) m/z 424 (M-H); HRMS (FAB+) for $C_{19}H_{24}NO_6S_2$ (M+H), calcd 426.1045, found 4.26.1056; Anal. Calcd for $C_{19}H_{23}NO_6S_2$: C, 56.63; H, 5.45; N, 3.29. Found: C, 53.48; H, 5.38; N, 3.29.

Step G: 11-(4-Methoxyphenylsulfonyl)-4,7,10,11,12,13-hexahydro-8-oxa-1-thia-11aza-cyclopentacylododecen-9-one

11-(4-Methoxyphenylsulfonyl)-4,7,10,11,12,13-hexahydro-8-oxa-1-thia-11aza-cyclopentacylododecen-9-one was prepared from N-(2-(3-(3-Hydroxybut-2-enyl)thiophen-2-yl) ethyl)-N-(4-methoxyphenylsulfonyl)aminoacetic acid (10:1 Z:E mixture, 0.57 g, 1.34 mmol) according to the same procedure used for the preparation of 10-(4-Methoxyphenylsulfonyl)-9,10,11,12-tetrahydro-6H-7-oxa-1-thia-10-aza-cyclopenta cycloundecen-8-one, using 2-chloro-1-methylpridinium iodide (1.37 g, 5.36 mmol), and triethylamine (1.5 ml, 10.8 mmol) in CH_3CN (200 ml). The residue was purified by flash chromatography (silica, 25 to 50% ethyl acetate in hexanes) to give the desired product as a white solid in a 9 to 1 ratio of cis to trans isomers. This product could be recrystallized from ethyl acetate-hexanes. Data for the major (cis) isomer: R_f = 0.38 (silica, 50% ethyl acetate in hexanes); mp 134-135°C (ethyl acetate-hexanes); MS (ESI, positive) m/z 408 (M+H), 425 ($M+NH_4$); HRMS (E1+) for $C_{19}H_{21}NO_5S_2$(M+), calcd 407.0861, found 407.0892; Anal. Calcd for $C_{19}H_{21}NO_5S_2$; C, 56.00; H, 5.19; N, 3.44. Found: C, 56.24; H, 5.14; N, 3.41.

<u>Step H: Methyl cis-(+/-)-7-(4-methoxyphenylsulfonyl)-5-vinyl-4,5,6,7,8,9-hexahydrothieno[2,3-*d*]azocine-6-carboxylate</u>

To a solution of a 9:1 Z:E mixture of 11-(4-methoxy phenylsulfonyl)-4,7,10,11,12,13-hexahydro-8-oxa-1-thia-11-aza-cyclopentacylododecen-9-one (748 mg, 1.84 mmol) dissolved in THF (18 ml) at -78°C was added TBSOTf (0.63 ml, 2.7 mmol) followed immediately by a 0.5 M solution of KHMDS in toluene (5.5 ml, 2.7 mmol). The reaction mixture was allowed to warm to about 0°C, over 10 minutes. The reaction mixture was then dilute with diethyl ether and poured onto pH 7 aqueous buffer solution. After addition of small volume of brine, the layers were separated and the organic layer was washed with brine, dried ($MgSO_4$) and concentrated to remove the

THF and diethyl either. This solution was diluted with additional toluene (13ml) and heated to 95°C for 2 h. The reaction mixture was then concentrated and the residue was dissolved in THF (2.5 ml) and methanol (10 ml) and treated with a 10% aqueous solution of K_2CO_3 (5.2 ml, 3.8 mmol). The mixture was stirred 1.5 h at room temperature and then concentrated to remove the THF and methanol. The residual aqueous mixture was diluted with H_2O and acidified with 2 N HCI (to pH 2) to give a white precipitate that was extracted into ethyl acetate. The organic phase was washed with brine, dried (Na_2SO_4) and concentrated to give cis-(+/-)-7-(4-methoxyphenyl sulfonyl)-5-vinyl-4,5,6,7,8,9-hexahydrothieno[2,3-*d*]azepine-6-carboxylic acid which was carried to the next step without further purification. A solution of the crude acid (860 mg) dissolved in benzene and methanol (2:1, 22 ml) at 0°C was added to a 2 M solution of $TMSCHN_2$ in hexanes (1.5 ml, 3 mmol). The reaction mixture was stirred 15 minutes and then the solvents were removed under reduced pressure. The reside was purified by flash chromatography (silica, 25% ethyl acetate in hexanes) to give the desired product. Recrystallization from dichloromethane-hexanes gave the crude product as a white solid: R_f = 0.50 (silica, 50% ethyl acetate in hexanes); R_f = 0.38 (silica, 10% ethyl acetate in toluene); mp 105-107°C (dicloromethane-hexanes); MS (ESI, positive) m/z 422 (M+H), 439 ($M+NH_4$); HRMS (EI+) for $C_{20}H_{23}NO_5S_2$ (M+), calcd 421.1018, found 421.1025; Anal. Calcd for $C_{20}H_{23}NO_5S_2$: C, 56.99; H, 5.50; N, 3.32. Found: C, 56.96; H, 5.58; N, 3.39.

<u>Step I: Methyl trans-(+/-)-7-(4-methoxyphenylsulfonyl)-5-phenethyl-4,5,6,7,8,9-hexahydro-thieno[2,3-*d*]azocine-6-carboxylate</u>

Methyl trans-(+/-)-7-(4-methoxyphenylsulfonyl)-5-phenethyl-4,5,6,7,8,9-hexahydro-thieno[2,3-*d*]azocine-6-carboxylate was prepared from methyl cis-(+/-)-7-(4-

methoxyphenylsulfonyl)-5-vinyl-4,5,6,7,8,9-hexahydro thieno[2,3-*d*]azepine-6-carboxylate (30 mg,71 mmol) according to the same procedure used for the preparation of methyl cis-(+/-)-6-(4-methoxyphenylsulfonyl)-4-phenethyl-5,6,7,8-tetrahydro-4*H*-thieno[2,3-*d*]azepine-5-carboxylate, using a 0.5 M solution of 9-BBN in THF (2.25 mL, 1.13 mmol) dissolved in THF (7 ml). This was followed by the addition of $PdCl_2(dppf)\bullet CH_2Cl_2$ (56 mg, 69 μmol), iodobenzene (0.66 ml, 5.9 mmol), K_2CO_3 (390 mg, 2.83 mmol), DMF (3 mL), and H_2O (0.6 mL). The residue was purified by flash chromatography (silica, 3% ethyl acetate in toluene) to give the desired product as a dark oil: R_f = 0.46 (silica, 10% ethyl acetate in toluene); MS (positive) m/z 500 (M+H), 517 ($M+NH_4$); HRMS (EI+) for $C_{26}H_{29}NO_5S_2$ (M+), calcd 499.41487, found 499.1446. This material was carried onto the next step without further purification.

Step J: trans-(+/-)-7-(4-Methoxyphenylsulfonyl)-5-phenethyl-4,5,6,7,8,9-hexahydro-thieno[2,3-*d*]azocine-6-carboxylic acid

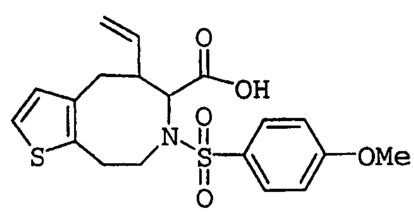
Trans-(+/-)-7-(4-methoxyphenylsulfonyl)-5-phenethyl-4,5,6,7,8,9-hexahydro-thieno[2,3-*d*]azocine-6-carboxylic acid was prepared from methyl trans-(+/-)-7-(4-methoxy phenylsulfonyl)-5-phenethyl-4,5,6,7,8,9-hexahydro-thieno [2,3-*d*]azocine-6-carboxylate (350 mg) according to the same procedure used for the preparation of trans-(+/-)-6-(4-methoxyphenylsulfonyl)-4-phenethyl-5,6,7,8-tetrahydro-4*H*-thieno[2,3-*d*]azepine-5-carboxylic acid, using 1 N LiOH (3.45 mL, 3.45 mmol) dissolved in THF:H_2O (3:1, 24 mL). The THF was removed *in vacuo* and the solids that remained in the aqueous layer were collected by filtration. These solids were suspended in water treated with 1 N HCl (to pH 2), and extracted into ethyl acetate. The organic layer was dried (Na_2SO_4) and concentrated to give the desired product as a white foam: R_f = 0.46 (silica, 10% methanol in

dichloromethane); MS (ESI, positive) m/z 503 ($M+NH_4$); MS (ESI, negative) m/z 484 (M-H); HRMS (EI+) for $C_{25}H_{27}NO_5S_2$ (M+), calcd 485.1331, found 485.1332; Anal. Calcd for $C_{25}H_{27}NO_5S_2$: C, 61.83; H, 5.60; N, 2.88. Found: C, 61.86; H, 5.81; N, 2.69.

Step K: trans-(+/-)-7-(4-Methoxyphenylsulfonyl)-5-phenethyl-4,5,6,7,8,9-hexahydrothieno[2,3-*d*]azocine-6-hydroxamic acid

trans-(+/-)-7-(4-Methoxyphenylsulfonyl)-5-phenethyl-4,5,6,7,8,9-hexahydrothieno[2,3-*d*]azocine-6-hydroxamic acid was prepared from trans-(+/-)-7-(4-methoxyphenyl sulfonyl)-5-phenethyl-4,5,6,7,8,9-hexahydrothieno[2,3-*d*]azocine-6-carboxylic acid (75 mg, 0.16 mmol) according to the same procedure used for the preparation of trans-(+/-)-6-(4-methoxyphenylsulfonyl)-4-phenethyl-5,6,7,8-tetrahydro-4*H*-thieno[2,3-*d*]azepine-5-hydroxamic acid, using hydroxylamine hydrochloride (79 mg, 1.1 mmol), diisopropylethylamine (265 µL, 1.52 mmol), and PyBroP (176 mg, 0.38 mmol) dissolved in dichloromethane (3 mL). The residue was purified by column chromatography (silica, 2.5% methanol in methylene chloride) to give the desired product as a white foam: R_f = 0.57 (silica, 7.5% methanol in dichloromethane); MS (positive) m/z 501 (M+H), 518 ($M+NH_4$); MS (negative) m/z 499 (M-H); HRMS (FAB+) for $C_{25}H_{29}N_2O_5S_2$ (M+H), calcd 501.1518, found 501.1528; Anal. Calcd for $C_{25}H_{28}N_2O_5S_2$: C, 59.98; H, 5.64; N, 5.60. Found C, 59.91; H, 5.71; N, 5.44.

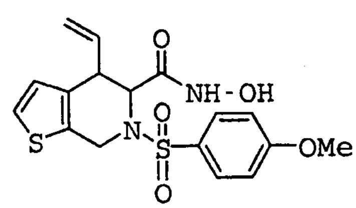
Example 69



Preparation of trans-(+/-)-7-(4-Methoxyphenylsulfonyl)-5-vinyl-4,5,6,7,8,9-hexahydrothieno[2,3-*d*]azepine-6-carboxylic acid and its methyl ester

trans-(+/-)-7-(4-Methoxyphenylsulfonyl)-5-vinyl-4,5,6,7,8,9-hexahydrothieno[2,3-*d*]azepine-6-carboxylic acid was prepared from methyl cis-(+/-)-7-(4-methoxy phenylsulfonyl)-5-vinyl-4,5,6,7,8,9-hexahydrothieno[2,3-*d*]azepine-6-carboxylate (28 mg, 66 mmol) according to the same procedure used for preparation of trans-(+/-)-6-(4-methoxyphenylsulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4H-thieno[2,3-*d*]azepine-5-carboxylic acid, using a 1M aqueous solution of LiOH (0.2 ml, 0.2 mmol) dissolved in THF and H_2O (3:1, 2 ml) to yield the desired product as a white foam: R_f = 0.5 (silica, 10% methanol in dichloromethane); MS (ESI, positive) m/z 408 (M+H), $(M+NH_4)^-$; MS (ESI, negative) m/z 406 (m-H); HRMS (EI+) for $C_{19}H_{21}NO_5S_2$ (M+), calcd 407.0861, found 407.0852. In order to confirm that the base has indeed induced epimerization, the methyl ester of the trans carboxylic acid was formed according to the same procedure used for the preparation of methyl trans-(+/-)-6-(4-Methoxyphenylsulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4H-thieno[2,3-*d*]azepine-5-carboxylate, using a 2 M solution of TMSCHN2 in hexanes (24 µL, 48 mmol) dissolved in benzene and methanol (2:1, 1.5 ml). The residue was purified by flash chromatography (silica, 25% ethyl acetate in hexanes) to give the desired ester as a white foam: R_f = 0.50 (silica 50% ethyl acetate in hexanes); MS (ESI, positive) m/z 422 (M+H), 439 $(M+NH_4)$; HRMS (EI+) for $C_{20}H_{23}NO_5S_2$ (M+), calcd 421.1018, found 421.1035.

<u>Example 70</u>



<u>Preparation of trans-(+/-)-6-(4-Methoxyphenylsulfonyl)-4-vinyl-4,5,6,7-tetrahydrothieno[2,3-c]pyridine-5-hydroxamic acid</u>

Step A: (3-Bromothiophen-2-yl)methanol

To a solution of the 3-bromo-2-formyl-thiophene (15 g, 78.5 mmol) dissolved in methanol and dichloromethane (3:2, 785 mL) was added the $NaBH_4$ (1.4 g, 38.2 mmol) in two portions. The mixture was stirred for 20 minutes, treated with 2 N HCl (10 mL), and then concentrated in vacuo. The residue was partitioned between ethyl acetate and H_2O. After separation, the aqueous layer was re-extracted with ethyl acetate. The combined organic layers were washed with 1 N HCl and brine, dried ($MgSO_4$), and concentrated to give the desired product as a yellow oil: R_f = 0.35 (silica 20% ethyl acetate in hexanes); MS (ESI, positive) m/z 211 ($M+NH_4$).

Step B: Methyl N-(3-Bromothiophen-2-yl)methyl-N-(4-methoxyphenylsulfonyl)aminoacetate

A solution of triphenylphosphine (30.9 g, 118 mmol) in THF (250 mL) was cooled to 0°C and treated with diisopropylazodicarboxylate (23.2 mL, 118 mmol). A precipitate formed as the reaction mixture stirred for 30 minutes. To this was added (3-bromothiophen-2-yl)methanol (15.1 g) dissolved in THF (80 mL), followed by addition of the methyl N-(4-methoxyphenylsulfonyl) aminoacetate (30.5 g, 118 mmol) dissolved in THF (155 mL). The resulting solution was warmed to ambient temperature and stirred for 24 h. The solvent was evaporated *in vacuo* and the residue was purified by flash chromatography (silica, 0 to 1% acetone in toluene) to give the desired product as a yellow solid. Trituration of this solid with hexanes gave a white solid: R_f = 0.5 (silica, 5% acetone in toluene); mp 96-99°C; MS (ESI, positive) m/z 434 (M+H, ^{79}Br), 436 (M+H, ^{81}Br), 451 ($M+NH_4$, ^{79}Br), 453 ($M+NH_4$, ^{81}Br); HRMS (FAB+) for $C_{15}H_{17}NO_5S_2Br$ (M+H, ^{79}Br), calcd 433.9732, found 433.9729; Anal. Calcd for $C_{15}H_{16}NO_5S_2Br$: C, 41.48; H, 3.71; N, 3.22. Found: C, 41.60; H, 3.65; N, 3.20.

Step C: Methyl N-(3-(3-(*tert*-Butyldimethylsilanyloxy)-propenyl)thiophen-2-yl)methyl)-N-(4-methoxyphenyl sulfonyl)aminoacetate

Methyl N-(3-(3-(*tert*-Butyldimethylsilanyloxy)-propenyl)thiophen-2-yl)methyl)-N-(4-methoxyphenyl sulfonyl)aminoacetate was prepared from methyl N-(3-bromothiophen-2-yl)methyl-N-(4-methoxyphenylsulfonyl) aminoacetate (1.56 g, 3.6 mmol) according to the same procedure used for the preparation of methyl N-(2-(3-(3-(*tert*-butyldimethylsilanyl oxy)propenyl)thiophen-2-yl)ethyl)-N-(4-methoxyphenyl sulfonyl)aminoacetate, using (Z)-$^{n}Bu_3SnCHCHCH_2OSi^{t}BuMe_2$ (20:1; Z:E) and $PdCl_2(PPh_3)_2$ (202 mg, 0.29 mmol) in toluene (21 mL). The residue was purified by flash chromatography (silica, 10 to 25% ethyl acetate in hexanes) to give the desired product as a yellow oil in a 20:1 ratio of cis to trans isomers. Data for the major (cis) isomer: R_f = 0.2 (silica, 20% ethyl acetate in hexanes); MS (ESI, positive) m/z 543 ($M+NH_4$); Anal. Calcd for $C_{24}H_{35}NO_6S_2Si$: C, 54.83; H, 6.71; N, 2.66. Found: C, 55.00; H, 6.85; N, 2.66.

Step D: N-((3-(3-Hydroxypropenyl)thiophen-2-yl)methyl)-N-(4-methoxyphenylsulfonyl)aminoacetic acid

N-((3-(3-Hydroxypropenyl)thiophen-2-yl)methyl)-N-(4-methoxyphenylsulfonyl)aminoacetic acid was prepared from methyl N-(3-(3-(*tert*-butyldimethylsilanyloxy)-propenyl)thiophen-2-yl)methyl)-N-(4-methoxyphenyl sulfonyl)aminoacetate (20:1 (Z:E) mixture, 1.55 g, 2.95 mmol) according to the same procedure used for the preparation of N-(2-(3-(3-(*tert*-butyldimethylsilanyloxy) propenyl)thiophen-2-yl)ethyl)-N-(4-methoxyphenyl sulfonyl)aminoacetic acid, using 1 N KOH (4.4 Ml) dissolved in THF (31 ml). The crude acid was carried onto the next step without purification: R_f = 0.5 (silica, 10% methanol in dichloromethane); MS (ESI,

negative) m/z 396 (M-Si^{t}BuMe$_2$), 510 (M-H). N-((3-(3-Hydroxypropenyl)thiophen-2-yl)methyl)-N-(4-methoxyphenylsulfonyl)aminoacetic acid was obtained according to the same procedure used for the preparation of N-(2-(3-(3-hydroxypropenyl)thiophen-2-yl) ethyl)-N-(4-methoxyphenylsulfonyl)aminoacetic acid, using the crude carboxylic acid (1.27 g) and a 1 M THF solution of TBAF (5 ml) dissolved in THF (23 ml). The residue was purified by flash chromatography (silica, ethyl acetate to 10% methanol in ethyl acetate with 1% acetic acid) to give the desired product as a tan solid in a 10 to 1 ratio of cis to trans isomers. Data for the major (cis) isomer: R_f = 0.25 (silica, 10% methanol in dichloromethane); MS (ESI, positive) m/z 415 (M+H); MS (ESI, negative) m/z 396 (M-H); HRMS (FAB+) for $C_{17}H_{20}NO_6S_2$ (M+H), calcd 298.0732, found 398.0806; Anal. Calcd for $C_{17}H_{19}NO_6S_2$: C, 51.37; H, 4.82; N, 3.52. Found: C, 51.17; H, 4.94; N, 3.49.

Step E: 10-(4-Methoxyphenylsulfonyl)-9,10,11,12-tetrahydro-6*H*-7oxa-1-thia-10-aza-cyclopentacycloundecen-8-one

10-(4-Methoxyphenylsulfonyl)-9,10,11,12-tetrahydro-6*H*-7oxa-1-thia-10-aza-cyclopentacycloundecen-8-one was prepared from N-((3-(3-Hydroxypropenyl)thiophen-2-yl) methyl)-N-(4-methoxyphenylsulfonyl)aminoacetic acid (10:1 (Z:E) mixture, 1.44 g, 3.6 mmol) according to the same procedure used for the preparation of 10-(4-methoxy phenylsulfonyl)-9,10,11,12-tetrahydro-6H-7-oxa-1-thia-10-aza-cyclopentacycloundecen-8-one, using 2-chloro-1-methylpyridinium iodide (3.6 g, 14.1 mmol), and triethylamine (3.9 mL, 28.1 mmol) in CH_3CN (518 mL). The residue was purified by flash chromatography (silica, 25 to 40% ethyl acetate in hexanes) to give the desired product as a white solid. This product could be recrystallized from ethyl acetate-hexanes: R_f = 0.42 (silica, 50% ethyl acetate in hexanes); mp 144-145°C

(ethyl acetate-hexanes); MS (ESI, positive) m/z 380 (M+H), 397 ($M+NH_4$); HRMS (EI+) for $C_{17}H_{17}NO_5S_2$: C, 53.81; H, 4.52; N, 3.69. Found: C, 53.92; H, 4.39; N, 3.64.

Step F: Methyl cis-(+/-)-6-(4-methoxyphenylsulfonyl)-4-vinyl-4,5,6,7-tetrahydro-thieno[2,3-*c*]pyridine-5-carboxylate

Methyl cis-(+/-)-6-(4-methoxyphenylsulfonyl)-4-vinyl-4,5,6,7-tetrahydro-thieno[2,3-*c*]pyridine-5-carboxylate was prepared from 10-(4-methoxyphenylsulfonyl)-9,10,11,12-tetrahydro-6*H*-7oxa-1-thia-10-aza-cyclopentacycloundecen-8-one (325 mg, 0.86 mmol) according to the same procedure used for the preparation of methyl cis-(+/-)-7-(4-methoxyphenylsulfonyl)-5-vinyl-4,5,6,7,8,9-hexahydrothieno[2,3-*d*]azocine-6-carboxylate, using TBDMSOTf (0.3 mL, 1.3 mmol), and a 0.5 M toluene solution of KHMDS (2.6 ml, 1.3 mmol) dissolved in THF (10 ml). After the buffered aqueous work-up, TLC indicated a mixture of the silyl ketene acetal (R_f = 0.66, silica, 50% ethyl acetate in hexanes) and the silyl ester (R_f = 0.66, silica, 50% ethyl acetate in hexanes). This was followed by treatment of the above solution with additional toluene (8 ml) and heating to 80°C for 1 h. The reaction mixture was then concentrated to give the crude silyl ester, which was dissolved in a mixture of methanol-THF (3:3:1, 6.5 ml) and treated with a 10% aqueous solution of K_2CO_3 (2.4 ml, 1.7 mmol). This gave the crude carboxylic acid (R_f = 0.32, silica, 10% methanol in dichloromethane), which was dissolved in benzene-methanol (2:1, 15 ml) and treated with a 2 M solution of $TMSCHN_2$ in hexanes (0.6 ml, 1.2 mmol), according to the same procedure referenced above. The residue was purified by flash chromatography (silica, 25% ethyl acetate in hexanes) to give the desired product as a white solid. This material could be recrystallized from dichloromethane-hexanes: R_f = 0.52 (silica, 50% ethyl acetate in

hexanes); mp 110-112°C (dichloromethane-hexanes); MS (ESI, positive) m/z 394 (M+H), 411 ($M+NH_4$); HRMS (FAB+) for $C_{18}H_{20}NO_5S_2$ (M+H), calcd 394.0783 found 394.0724; Anal Calcd $C_{18}H_{19}NO_5S_2$: C, 54.94; H, 4.87; N, 3.56. Found: C, 55.06; H, 4.86; N, 3.62.

Step G: trans-(+/-)-6-(4-Methoxyphenylsulfonyl)-4-vinyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-5-carboxylic acid

trans-(+/-)-6-(4-Methoxyphenylsulfonyl)-4-vinyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-5-carboxylic acid was prepared from methyl cis-(+/-)-6-(4-methoxyphenyl sulfonyl)-4-vinyl-4,5,6,7-tetrahydro-thieno[2,3-*c*]pyridine-5-carboxylate (138 mg, 0.35 mol) according to the same procedure used for the preparation of trans-(+/-)-6-(4-Methoxyphenylsulfonyl)-4-phenethyl-5,6,7,8-tetrahydro-4*H*-thieno[2,3-*d*]azepine-5-carboxylic acid, using a 1 M aqueous solution of LiOH (1.05 ml, 1.05 mmol) dissolved in THF and H_2O (3:1, 8 ml). This gave the desired product as a white foam: R_f = 0.25 (silica, 10% methanol in dichloromethane); MS (ESI, positive) m/z 380 (M+H), 397 ($M+NH_4$); MS (ESI, negative) m/z 378 (M-H) HRMS (FAB+) for $C_{20}H_{23}NO_5S_2$ (M+H), calcd 380.0626, found 380.0681. The cis acid (6 mg, 5%) was also obtained as a clear oil: R_f = 0.32 (silica, 10% methanol in dichloromethane); MS (ESI, positive) m/z 380 (M+H), 397 ($M+NH_4$); MS (ESI, negative) m/z 378 (M-H).

Step H: trans-(+/-)-6-(4-Methoxyphenylsulfonyl)-4-vinyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-5-hydroxamic acid

trans-(+/-)-6-(4-Methoxyphenylsulfonyl)-4-vinyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-5-hydroxamic acid was prepared from trans-(+/-)-6-(4-methoxyphenylsulfonyl)-4-vinyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-5-carboxylic acid (60 mg, 0.16 mmol) according to the same procedure used for the preparation of trans-(+/-)-6-(4-

Methoxyphenylsulfonyl)-4-phenethyl-5,6,7,8-tetrahydro-4*H*-thieno[2,3-*d*]azepine-5-hydroxamic acid, using hydroxylamine hydrochloride (33 mg, 0.47 mmol), diisopropylethylamine (110 µl, 0.63 mmol), and PyBroP (90 mg, 0.19 mmol) dissolved in dichloromethane (3 ml). The residue was purified by column chromatography (silica, 2.5 to 5% methanol in methylene chloride) to give the desired product as a white foam. This material could be triturated with diethyl ether and then recrystallized from dichloromethane-hexanes to give pure product: R_f = 0.44 (silica, 10% methanol in dichloromethane); mp 145.5-147.5°C; MS (ESI, negative) m/z 393 (M-H); MS (ESI, negative) m/z 393 (M-H) (FAB+) for $C_{17}H_{19}N_2O_5S_2$ (M+H), calcd 395.0735, found 395.0721.

Example 71

Utilizing the procedures of Examples 1-70, the compounds of Table III can be prepared.

TABLE III

4-trans-isopropyl-6-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[2,3,-c]pyridine-5-hydroxamic acid

4-trans-isopropyl-6-(4-chlorophenylsulfonyl)-4,5,6,7-tetrahydro-thieno[2,3,-c]pyridine-5-hydroxamic acid

4-trans-phenethyl-6-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[2,3,-c]pyridine-5-hydroxamic acid

4-trans-phenethyl-6-(4-fluorophenylsulfonyl)-4,5,6,7-tetrahydro-thieno[2,3,-c]pyridine-5-hydroxamic acid

4-trans-hydroxymethyl-6-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[2,3,-c]pyridine-5-hydroxamic acid

4-trans-(4-biphenylbenzyl)-6-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[2,3,-c]pyridine-5-hydroxamic acid

4-trans-isopropyl-6-(4-chlorophenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid

4-trans-butyl-6-(4-chlorophenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid

4-trans-(4-bromobenzyl)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid

4-trans-(4-fluorobenzyl)-6-(4-fluorophenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid

4-trans-isobutyl-8-cis-hydroxy-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid

4-cis-isobutyl-8-cis-hydroxy-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid

4-trans-(4-phenylbenzyl)-8-cis-hydroxy-6-(4-methoxy phenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d] azepine-5-hydroxamic acid

4-cis-(4-phenylbenzyl)-8-cis-hydroxy-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid

4-trans-(4-pyridinebenzyl)-8-cis-hydroxy-6-(4-methoxy phenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid

4-cis-(4-pyridinebenzyl)-8-cis-hydroxy-6-(4-methoxy phenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d] azepine-5-hydroxamic acid

4-trans-(4-bromobenzyl)-6-(3-chlorophenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid

4-trans-(4-fluorobenzyl)-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid

4-trans-isobutyl-8-cis-hydroxy-6-(4-nitrophenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid

4-cis-isobutyl-8-cis-hydroxy-6-(3-chlorophenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid

4-trans-(4-phenylbenzyl)-8-cis-hydroxy-6-(3-pyridinephenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid

4-cis-(4-phenylbenzyl)-8-cis-hydroxy-6-(3-chlorophenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid

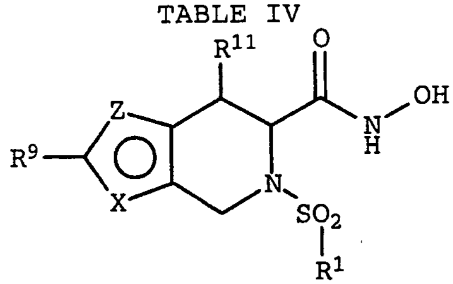
4-trans-(4-pyridinebenzyl)-8-cis-hydroxy-6-(2-fluorophenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid

4-cis-(4-pyridinebenzyl)-8-cis-hydroxy-6-(4-nitrophenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid

Example 72

Using the procedures of the above general descriptions and the above examples, the compounds of Tables IV-X can be prepared.

TABLE IV



X	Z	R^1	R^9	R^{11}
C-H	S	4-MeO-Ph-	BzMeN-C(O)-	(cis)HO-
C-H	S	4-MeO-Ph-	phenyl	(cis)HO-
C-H	S	4-MeO-Ph-	MeO-C(O)-	(cis)HO-
C-H	S	4-MeO-Ph-	HO-C(O)-	(cis)HO-
C-H	S	4-MeO-Ph-	EtO-C(O)-	(cis)HO-
C-H	S	4-MeO-Ph-	2-pyridyl	(cis)HO-
C-H	S	4-MeO-Ph-	3-pyridyl	(cis)HO-
C-H	S	4-MeO-Ph-	4-morpholino-C(O)-	(cis)HO-
C-H	S	4-MeO-Ph-	BzO-C(O)-	(cis)HO-
C-H	S	4-MeO-Ph-	Ph-NH-C(O)-	(cis)HO-
C-H	S	4-MeO-Ph-	Bz-NH-C(O)-	(cis)HO-

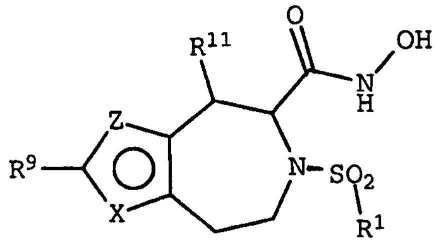
C-H	S	4-MeO-Ph-	3-Ph-propyl-NH-C(O)-	(cis)HO-
C-H	S	4-MeO-Ph-	(2-Ph-ethyl)(Me)N-C(O)-	(cis)HO-
C-H	S	4-MeO-Ph-	BzEtN-C(O)-	(cis)HO-
C-H	S	4-MeO-Ph-	(4,4-dimethyl pentyl)NHC(O)-	(cis)HO-
C-H	S	4-MeO-Ph-	(4,4-diphenyl butyl)NHC(O)-	(cis)HO-
C-H	S	4-MeO-Ph-	PhMeN-C(O)-	(cis)HO-
C-H	S	4-MeO-Ph-	PhMeN-C(O)-	(trans)HO-
C-H	S	4-MeO-Ph-	H-	BzNH-C(O)-O-
C-H	S	4-MeO-Ph-	H-	PhNH-C(O)-O-
C-H	S	4-MeO-Ph-	H-	MeNH-C(O)-O-
C-H	S	4-MeO-Ph-	H-	i-propylNH-C(O)-O-
C-H	S	4-MeO-Ph-	H-	(4-PhO-Ph)NH-C(O)-O-
C-H	S	4-MeO-Ph-	H-	(1-Ph-ethyl)NH-C(O)-O-
C-H	S	4-MeO-Ph-	H-	(4-MeO-Ph)NH-C(O)-O-
C-H	S	4-MeO-Ph-	H-	(2-Ph-ethyl)NH-C(O)-O-
C-H	S	phenyl	H-	HO-
C-H	S	4-CN-Ph-	H-	HO-
C-H	S	4-(Me-C(O)-NH)-Ph-	H-	HO-
C-H	S	4-i-propyl-Ph-	H-	HO-
C-H	S	4-Et-Ph-	H-	HO-

C-H	S	4-t-butyl-Ph-	H-	H-
C-H	S	n-dodecyl	H-	HO-
C-H	S	n-octyl	H-	H-
N	S	4-MeO-Ph-	Ph-SO_2-NH-	H-
N	S	4-MeO-Ph-	MeC(O)-NH-	HO-
N	S	4-MeO-Ph-	MeO-C(O)-NH-	(4-F-Ph)NH-C(O)-O-
S	N	4-MeO-Ph-	methyl	H-
S	N	4-MeO-Ph-	Ph-C(O)-NH-	HO-
S	N	4-MeO-Ph-	H-	benzyl
S	N	4-MeO-Ph-	H-	HO-
S	N	4-MeO-Ph-	H-	PhNH-C(O)-O-
S	N	4-MeO-Ph-	methyl	PhNH-C(O)-O-
S	N	4-MeO-Ph-	H-	H-
N	S	4-MeO-Ph-	H-	H-
C-H	O	4-MeO-Ph-	H-	H-
C-H	O	4-MeO-Ph-	EtO-C(O)-	H-
C-H	O	4-MeO-Ph-	H-	HO-
C-H	O	4-MeO-Ph-	H-	PhNH-C(O)-O-
C-H	O	4-MeO-Ph-	methyl	PhNH-C(O)-O-
S	C-H	4-MeS-Ph-	BzMeN-C(O)-	HO-
S	C-H	4-Cl-Ph-	phenyl	Ph-SO_2-NH-
S	C-H	4-CF_3O-Ph-	MeO-C(O)-	2-thienyl-S-
S	C-H	5-benzo-dioxolyl	HO-C(O)-	HO-
S	C-H	4-Me-Ph-	2-pyridyl	HO-
S	C-H	4-MeO-Ph-	3-pyridyl	MeS-

S	C-H	4-MeO-Ph-	4-morpholino-C(O)-	HO-
S	C-H	n-dodecyl	BzO-C(O)-	HO-
S	C-H	4-MeO-Ph-	Ph-NH-C(O)-	3-thienyl-NH-C(O)-O-
S	C-H	2-furyl	Bz-NH-C(O)-	HO-
S	C-H	4-MeO-Ph-	3-Ph-propyl-NH-C(O)-	2-pyridyl-NH-C(O)-O-
S	C-H	4-PhO-Ph-	(2-Ph-ethyl)(Me)N-C(O)-	HO-
S	C-H	4-pyridyl	BzEtN-C(O)-	propargyl
S	C-H	4-MeO-Ph-	(4,4-dimethyl pentyl)NHC(O)-	2-thienyl-O-
O	C-H	4-MeO-Ph-	3-pyridyl	HO-
O	C-H	5-benzofuranyl	4-morpholino-C(O)-	HO-
O	C-H	4-MeO-Ph-	BzO-C(O)-	HO-
O	C-H	5-benzo-thiazolyl	Ph-NH-C(O)-	(1-Ph-ethyl)NH-C(O)-O-
O	C-H	4-MeO-Ph-	Bz-NH-C(O)-	HO-
O	C-H	4-PhO-Ph-	3-Ph-propyl-NH-C(O)-	HO-
O	C-H	4-MeO-Ph-	(2-Ph-ethyl)(Me)N-C(O)-	vinyl
O	C-H	n-dodecyl	BzEtN-C(O)-	HO-
O	C-H	4-MeO-Ph-	(4,4-dimethyl pentyl)NHC(O)-	PhNH-C(O)-O-
N	S	4-morpholino	phenyl	PhNH-C(O)-O-
N	S	2-naphthyl	3-pyridyl	MeNH-C(O)-O-
N	S	3,4-dimethoxy-	4-morpholino-	i-propylNH-

		phenyl	C(O)-	C(O)-O-
S	N	4-piperidinyl-butyl	BzO-C(O)-	(4-PhO-Ph)NH-C(O)-O-
S	N	6-benzo-dioxanyl	Ph-NH-C(O)-	2-thienyl-NH-C(O)-O-
S	N	4-hydroxy-cyclohexyl	2-pyridyl-NH-C(O)-	(4-MeO-Ph)NH-C(O)-O-
C-H	S	4-MeO-Ph-	BzMeN-C(O)-	3-(3-furyl)-butyl
C-H	S	4-MeO-Ph-	4-acetamido-phenyl	4-methyl-pentyl
C-H	S	4-MeO-Ph-	3-pyridyl	2-MeS-ethyl
C-H	S	4-MeO-Ph-	H-	PhNH-C(O)-ethyl
S	C-H	4-MeO-Ph-	4-chlorobenzyl	4-pyrid-3-yl-butyl
S	C-H	4-MeO-Ph-	4-pyridyl	3-hydroxy-butyl
S	C-H	4-MeO-Ph-	H-	PhNH-C(O)-CH_2-
S	C-H	4-MeO-Ph-	HO-C(O)-	2-(pyrid-3-yl-C(O)-NH)-ethyl
N	S	4-MeO-Ph-	phenyl	2-(2-thienyl-thio)ethyl
N	S	4-MeO-Ph-	4-morpholino-C(O)-	PhNH-C(O)-methyl
N	S	4-MeO-Ph-	3-pyridyl	3-MeS-propyl
S	N	4-MeO-Ph-	EtO-C(O)-	2-phenoxyethyl
S	N	4-MeO-Ph-	Ph-NH-C(O)-	3-pyrid-3-yl-propyl
S	N	4-MeO-Ph-	2-pyridyl-NH-C(O)-	iso-butyl

TABLE V



X	Z	R^1	R^9	R^{11}
C-H	S	4-MeO-Ph-	BzMeN-C(O)-	HO-
C-H	S	4-MeO-Ph-	phenyl	HO-
C-H	S	4-MeO-Ph-	EtO-C(O)-	HO-
C-H	S	4-MeO-Ph-	HO-C(O)-	HO-
C-H	S	4-MeO-Ph-	2-pyridyl	HO-
C-H	S	4-CF_3O-Ph-	3-pyridyl	H-
C-H	S	4-MeO-Ph-	4-morpholino-C(O)-	HO-
C-H	S	4-MeO-Ph-	BzO-C(O)-	HO-
C-H	S	4-Me-Ph-	Ph-NH-C(O)-	HO-
C-H	S	3-MeO-Ph-	Bz-NH-C(O)-	HO-
C-H	S	4-MeO-Ph-	BzEtN-C(O)-	HO-
C-H	S	4-MeO-Ph-	(4,4-dimethyl pentyl)NHC(O)-	HO-
C-H	S	4-Cl-Ph-	PhMeN-C(O)-	HO-
C-H	S	2-thienyl	PhMeN-C(O)-	HO-
C-H	S	4-MeO-Ph-	H-	BzNH-C(O)-O-
C-H	S	3,4-dimethoxy-phenyl	H-	PhNH-C(O)-O-
C-H	S	4-MeO-Ph-	H-	(4-PhO-Ph)NH-C(O)-O-
C-H	S	4-MeO-Ph-	H-	i-propylNH-

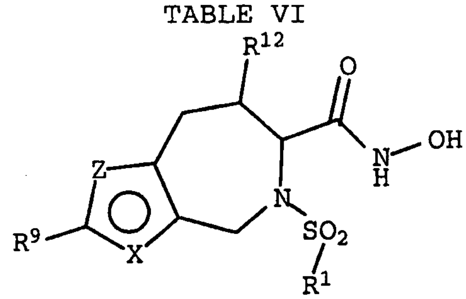
				C(O)-O-
C-H	S	4-MeO-Ph-	H-	MeNH-C(O)-O-
C-H	S	4-MeO-Ph-	H-	(1-Ph-ethyl) NH-C(O)-O-
C-H	S	4-MeO-Ph-	H-	(4-MeO-Ph)NH-C(O)-O-
C-H	S	5-benzo-thiazolyl	H-	(2-Ph-ethyl) NH-C(O)-O-
C-H	S	phenyl	H-	vinyl-
C-H	S	4-CN-Ph-	H-	HO-
C-H	S	4-(Me-C(O)-NH)-Ph-	H-	HO-
C-H	S	4-i-propyl-Ph-	H-	HO-
C-H	S	4-Et-Ph-	H-	HO-
C-H	S	4-t-butyl-Ph-	H-	H-
C-H	S	n-dodecyl	H-	HO-
C-H	S	n-octyl	H-	H-
N	S	4-MeO-Ph-	Ph-SO_2-NH-	H-
N	S	4-MeO-Ph-	MeC(O)-NH-	HO-
N	S	4-MeO-Ph-	MeO-C(O)-NH-	(4-F-Ph)NH-C(O)-O-,
S	N	4-MeO-Ph-	methyl	H-
S	N	4-MeO-Ph-	Ph-C(O)-NH-	HO-
S	N	4-MeO-Ph-	H-	benzyl
S	N	4-MeO-Ph-	H-	HO-
S	N	4-MeO-Ph-	H-	PhNH-C(O)-O-
S	N	4-MeO-Ph-	methyl	PhNH-C(O)-O-
S	N	4-MeO-Ph-	H-	H-
N	S	4-MeO-Ph-	H-	H-

C-H	O	4-MeO-Ph-	H-	H-
C-H	O	4-MeO-Ph-	EtO-C(O)-	H-
C-H	O	4-MeO-Ph-	H-	HO-
C-H	O	4-MeO-Ph-	H-	PhNH-C(O)-O-
C-H	O	4-MeO-Ph-	methyl	PhNH-C(O)-O-
S	C-H	4-MeS-Ph-	BzMeN-C(O)-	HO-
S	C-H	4-Cl-Ph-	phenyl	Ph-SO_2-NH-
S	C-H	4-CF_3O-Ph-	MeO-C(O)-	thienyl-S-
S	C-H	5-benzo-dioxolyl	HO-C(O)-	HO-
S	C-H	4-Me-Ph-	2-pyridyl	HO-
S	C-H	4-MeO-Ph-	3-pyridyl	MeS-
S	C-H	4-MeO-Ph-	4-morpholino-C(O)-	HO-
S	C-H	n-dodecyl	BzO-C(O)-	HO-
S	C-H	4-MeO-Ph-	Ph-NH-C(O)-	thienyl-NH-C(O)-O-
S	C-H	furyl	Bz-NH-C(O)-	HO-
S	C-H	4-MeO-Ph-	3-Ph-propyl-NH-C(O)-	2-pyridyl-NH-C(O)-O-
S	C-H	4-PhO-Ph-	(2-Ph-ethyl)(Me)N-C(O)-	HO-
S	C-H	4-pyridyl	BzEtN-C(O)-	propargyl
S	C-H	4-MeO-Ph-	(4,4-dimethyl pentyl)NHC(O)-	thienyl-O-
O	C-H	4-MeO-Ph-	3-pyridyl	HO-
O	C-H	5-benzofuranyl	4-morpholino-C(O)-	HO-
O	C-H	4-MeO-Ph-	BzO-C(O)-	HO-

O	C-H	4-MeO-Ph-	Bz-NH-C(O)-	HO-
O	C-H	5-benzo-thiazolyl	Ph-NH-C(O)-	(1-Ph-ethyl) NH-C(O)-O-
O	C-H	4-PhO-Ph-	3-Ph-propyl-NH-C(O)-	HO-
O	C-H	4-MeO-Ph-	(2-Ph-ethyl) (Me)N-C(O)-	vinyl
O	C-H	4-MeO-Ph-	(4,4-dimethyl pentyl)NHC(O)-	PhNH-C(O)-O-
O	C-H	n-dodecyl	BzEtN-C(O)-	HO-
N	S	4-morpholino	phenyl	PhNH-C(O)-O-
N	S	2-naphthyl	3-pyridyl	MeNH-C(O)-O-
N	S	3,4-dimethoxy-phenyl	4-morpholino-C(O)-	i-propylNH-C(O)-O-
S	N	4-piperidinyl-butyl	BzO-C(O)-	(4-PhO-Ph)NH-C(O)-O-
S	N	6-benzo-dioxanyl	Ph-NH-C(O)-	thienyl-NH-C(O)-O-
S	N	4-hydroxy-cyclohexyl	2-pyridyl-NH-C(O)-	(4-MeO-Ph)NH-C(O)-O-
C-H	S	4-MeO-Ph-	BzMeN-C(O)-	3-(3-furyl)-butyl
C-H	S	4-MeO-Ph-	4-acetamido-phenyl	4-methyl-pentyl
C-H	S	4-MeO-Ph-	3-pyridyl	2-MeS-ethyl
C-H	S	4-MeO-Ph-	H-	PhNH-C(O)-ethyl
S	C-H	4-MeO-Ph-	4-chlorobenzyl	4-pyrid-3-yl-butyl
S	C-H	4-MeO-Ph-	4-pyridyl	3-hydroxy-butyl

S	C-H	4-MeO-Ph-	H-	PhNH-C(O)-methyl
S	C-H	4-MeO-Ph-	HO-C(O)-	2-(pyrid-3-yl-C(O)-NH)-ethyl
N	S	4-MeO-Ph-	phenyl	2-(2-thienyl-thio)ethyl
N	S	4-MeO-Ph-	3-pyridyl	3-MeS-propyl
N	S	4-MeO-Ph-	4-morpholino-C(O)-	PhNH-C(O)-methyl
S	N	4-MeO-Ph-	EtO-C(O)-	2-phenoxyethyl
S	N	4-MeO-Ph-	Ph-NH-C(O)-	3-pyrid-3-yl-propyl
S	N	4-MeO-Ph-	2-pyridyl-NH-C(O)-	iso-butyl

TABLE VI



X	Z	R^1	R^9	R^{12}
C-H	S	4-MeO-Ph-	BzMeN-C(O)-	HO-
C-H	S	4-MeO-Ph-	phenyl	HO-
C-H	S	4-MeO-Ph-	EtO-C(O)-	HO-
C-H	S	4-MeO-Ph-	HO-C(O)-	HO-
C-H	S	4-MeO-Ph-	2-pyridyl	HO-
C-H	S	4-CF_3O-Ph-	3-pyridyl	H-
C-H	S	4-MeO-Ph-	4-morpholino-C(O)-	HO-

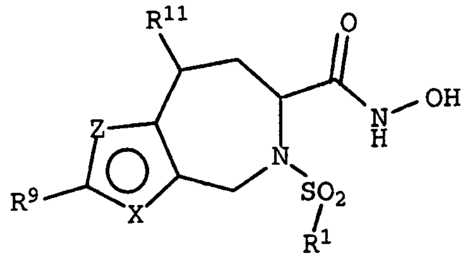
C-H	S	4-MeO-Ph-	BzO-C(O)-	HO-
C-H	S	4-Me-Ph-	Ph-NH-C(O)-	HO-
C-H	S	3-MeO-Ph-	Bz-NH-C(O)-	HO-
C-H	S	4-MeO-Ph-	BzEtN-C(O)-	HO-
C-H	S	4-MeO-Ph-	(4,4-dimethyl pentyl)NHC(O)-	HO-
C-H	S	4-Cl-Ph-	PhMeN-C(O)-	HO-
C-H	S	2-thienyl	PhMeN-C(O)-	HO-
C-H	S	4-MeO-Ph-	H-	BzNH-C(O)-O-
C-H	S	3,4-dimethoxy-phenyl	H-	PhNH-C(O)-O-
C-H	S	4-MeO-Ph-	H-	MeNH-C(O)-O-
C-H	S	4-MeO-Ph-	H-	i-propylNH-C(O)-O-
C-H	S	4-MeO-Ph-	H-	(4-PhO-Ph)NH-C(O)-O-
C-H	S	4-MeO-Ph-	H-	(1-Ph-ethyl) NH-C(O)-O-
C-H	S	4-MeO-Ph-	H-	(4-MeO-Ph)NH-C(O)-O-
C-H	S	5-benzo-thiazolyl	H-	(2-Ph-ethyl) NH-C(O)-O-
C-H	S	phenyl	H-	vinyl-
C-H	S	4-CN-Ph-	H-	HO-
C-H	S	4-(Me-C(O)-NH)-Ph-	H-	HO-
C-H	S	4-i-propyl-Ph-	H-	HO-
C-H	S	4-Et-Ph-	H-	HO-
C-H	S	4-t-butyl-Ph-	H-	H-
C-H	S	n-dodecyl	H-	HO-

C-H	S	n-octyl	H-	H-
N	S	4-MeO-Ph-	Ph-SO_2-NH-	H-
N	S	4-MeO-Ph-	MeC(O)-NH-	HO-
N	S	4-MeO-Ph-	MeO-C(O)-NH-	(4-F-Ph)NH-C(O)-O-
S	N	4-MeO-Ph-	methyl	H-
S	N	4-MeO-Ph-	Ph-C(O)-NH-	HO-
S	N	4-MeO-Ph-	H-	benzyl
S	N	4-MeO-Ph-	H-	HO-
S	N	4-MeO-Ph-	H-	PhNH-C(O)-O-
S	N	4-MeO-Ph-	methyl	PhNH-C(O)-O-
S	N	4-MeO-Ph-	H-	H-
N	S	4-MeO-Ph-	H-	H-
C-H	O	4-MeO-Ph-	H-	H-
C-H	O	4-MeO-Ph-	EtO-C(O)-	H-
C-H	O	4-MeO-Ph-	H-	HO-
C-H	O	4-MeO-Ph-	H-	PhNH-C(O)-O-
C-H	O	4-MeO-Ph-	methyl	PhNH-C(O)-O-
S	C-H	4-MeS-Ph-	BzMeN-C(O)-	HO-
S	C-H	4-Cl-Ph-	phenyl	Ph-SO_2-NH-
S	C-H	4-CF_3O-Ph-	MeO-C(O)-	thienyl-S-
S	C-H	5-benzo-dioxolyl	HO-C(O)-	HO-
S	C-H	4-Me-Ph-	2-pyridyl	HO-
S	C-H	4-MeO-Ph-	3-pyridyl	MeS-
S	C-H	4-MeO-Ph-	4-morpholino-C(O)-	HO-
S	C-H	n-dodecyl	BzO-C(O)-	HO-

S	C-H	4-MeO-Ph-	Ph-NH-C(O)-	thienyl-NH-C(O)-O-
S	C-H	furyl	Bz-NH-C(O)-	HO-
S	C-H	4-MeO-Ph-	3-Ph-propyl-NH-C(O)-	2-pyridyl-NH-C(O)-O-
S	C-H	4-PhO-Ph-	(2-Ph-ethyl)(Me)N-C(O)-	HO-
S	C-H	4-pyridyl	BzEtN-C(O)-	propargyl
S	C-H	4-MeO-Ph-	(4,4-dimethyl pentyl)NHC(O)-	thienyl-O-
O	C-H	4-MeO-Ph-	3-pyridyl	HO-
O	C-H	5-benzofuranyl	4-morpholino-C(O)-	HO-
O	C-H	4-MeO-Ph-	BzO-C(O)-	HO-
O	C-H	5-benzo-thiazolyl	Ph-NH-C(O)-	(1-Ph-ethyl)NH-C(O)-O-
O	C-H	4-MeO-Ph-	Bz-NH-C(O)-	HO-
O	C-H	4-PhO-Ph-	3-Ph-propyl-NH-C(O)-	HO-
O	C-H	4-MeO-Ph-	(2-Ph-ethyl)(Me)N-C(O)-	vinyl
O	C-H	n-dodecyl	BzEtN-C(O)-	HO-
O	C-H	4-MeO-Ph-	(4,4-dimethyl pentyl)NHC(O)-	PhNH-C(O)-O-
N	S	4-morpholino	phenyl	PhNH-C(O)-O-
N	S	2-naphthyl	3-pyridyl	MeNH-C(O)-O-
N	S	3,4-dimethoxy-phenyl	4-morpholino-C(O)-	i-propylNH-C(O)-O-
S	N	4-piperidinyl-butyl	BzO-C(O)-	(4-PhO-Ph)NH-C(O)-O-

S	N	6-benzo-dioxanyl	Ph-NH-C(O)-	thienyl-NH-C(O)-O-
S	N	4-hydroxy-cyclohexyl	2-pyridyl-NH-C(O)-	(4-MeO-Ph)NH-C(O)-O-
C-H	S	4-MeO-Ph-	BzMeN-C(O)-	3-(3-furyl)-butyl
C-H	S	4-MeO-Ph-	4-acetamido-phenyl	4-methyl-pentyl
C-H	S	4-MeO-Ph-	3-pyridyl	2-MeS-ethyl
C-H	S	4-MeO-Ph-	H-	PhNH-C(O)-ethyl
S	C-H	4-MeO-Ph-	4-chlorobenzyl	4-pyrid-3-yl-butyl
S	C-H	4-MeO-Ph-	4-pyridyl	3-hydroxy-butyl
S	C-H	4-MeO-Ph-	H-	PhNH-C(O)-methyl
S	C-H	4-MeO-Ph-	HO-C(O)-	2-(pyrid-3-yl-C(O)-NH)-ethyl
N	S	4-MeO-Ph-	phenyl	2-(2-thienyl-thio)ethyl
N	S	4-MeO-Ph-	4-morpholino-C(O)-	PhNH-C(O)-methyl
N	S	4-MeO-Ph-	3-pyridyl	3-MeS-propyl
S	N	4-MeO-Ph-	EtO-C(O)-	2-phenoxyethyl
S	N	4-MeO-Ph-	Ph-NH-C(O)-	3-pyrid-3-yl-propyl
S	N	4-MeO-Ph-	2-pyridyl-NH-C(O)-	iso-butyl

TABLE VII



X	Z	R^1	R^9	R^{11}
C-H	S	4-MeO-Ph-	BzMeN-C(O)-	HO-
C-H	S	4-MeO-Ph-	phenyl	HO-
C-H	S	4-MeO-Ph-	EtO-C(O)-	HO-
C-H	S	4-MeO-Ph-	HO-C(O)-	HO-
C-H	S	4-MeO-Ph-	2-pyridyl	HO-
C-H	S	4-CF_3O-Ph-	3-pyridyl	H-
C-H	S	4-MeO-Ph-	4-morpholino-C(O)-	HO-
C-H	S	4-MeO-Ph-	BzO-C(O)-	HO-
C-H	S	4-Me-Ph-	Ph-NH-C(O)-	HO-
C-H	S	3-MeO-Ph-	Bz-NH-C(O)-	HO-
C-H	S	4-MeO-Ph-	BzEtN-C(O)-	HO-
C-H	S	4-MeO-Ph-	(4,4-dimethyl pentyl)NHC(O)-	HO-
C-H	S	4-Cl-Ph-	PhMeN-C(O)-	HO-
C-H	S	2-thienyl	PhMeN-C(O)-	HO-
C-H	S	4-MeO-Ph-	H-	BzNH-C(O)-O-
C-H	S	3,4-dimethoxy-phenyl	H-	PhNH-C(O)-O-
C-H	S	4-MeO-Ph-	H-	MeNH-C(O)-O-
C-H	S	4-MeO-Ph-	H-	i-propylNH-C(O)-O-
C-H	S	4-MeO-Ph-	H-	(4-PhO-Ph)NH-

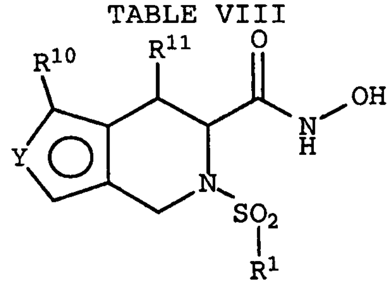
				C(O)-O-
C-H	S	4-MeO-Ph-	H-	(1-Ph-ethyl) NH-C(O)-O-
C-H	S	4-MeO-Ph-	H-	(4-MeO-Ph)NH-C(O)-O-
C-H	S	5-benzo-thiazolyl	H-	(2-Ph-ethyl) NH-C(O)-O-
C-H	S	phenyl	H-	vinyl-
C-H	S	4-CN-Ph-	H-	HO-
C-H	S	4-(Me-C(O)-NH)-Ph-	H-	HO-
C-H	S	4-i-propyl-Ph-	H-	HO-
C-H	S	4-Et-Ph-	H-	HO-
C-H	S	4-t-butyl-Ph-	H-	H-
C-H	S	n-dodecyl	H-	HO-
C-H	S	n-octyl	H-	H-
N	S	4-MeO-Ph-	Ph-SO_2-NH-	H-
N	S	4-MeO-Ph-	MeC(O)-NH-	HO-
N	S	4-MeO-Ph-	MeO-C(O)-NH-	(4-F-Ph)NH-C(O)-O-
S	N	4-MeO-Ph-	methyl	H-
S	N	4-MeO-Ph-	Ph-C(O)-NH-	HO-
S	N	4-MeO-Ph-	H-	benzyl
S	N	4-MeO-Ph-	H-	HO-
S	N	4-MeO-Ph-	H-	PhNH-C(O)-O-
S	N	4-MeO-Ph-	methyl	PhNH-C(O)-O-
S	N	4-MeO-Ph-	H-	H-
N	S	4-MeO-Ph-	H-	H-
C-H	O	4-MeO-Ph-	H-	H-

C-H	O	4-MeO-Ph-	EtO-C(O)-	H-
C-H	O	4-MeO-Ph-	H-	HO-
C-H	O	4-MeO-Ph-	H-	PhNH-C(O)-O-
C-H	O	4-MeO-Ph-	methyl	PhNH-C(O)-O-
S	C-H	4-MeS-Ph-	BzMeN-C(O)-	HO-
S	C-H	4-Cl-Ph-	phenyl	Ph-SO_2-NH-
S	C-H	4-CF_3O-Ph-	MeO-C(O)-	thienyl-S-
S	C-H	5-benzo-dioxolyl	HO-C(O)-	HO-
S	C-H	4-Me-Ph-	2-pyridyl	HO-
S	C-H	4-MeO-Ph-	3-pyridyl	MeS-
S	C-H	4-MeO-Ph-	4-morpholino-C(O)-	HO-
S	C-H	n-dodecyl	BzO-C(O)-	HO-
S	C-H	4-MeO-Ph-	Ph-NH-C(O)-	thienyl-NH-C(O)-O-
S	C-H	furyl	Bz-NH-C(O)-	HO-
S	C-H	4-MeO-Ph-	3-Ph-propyl-NH-C(O)-	2-pyridyl-NH-C(O)-O-
S	C-H	4-pyridyl	BzEtN-C(O)-	propargyl
S	C-H	4-PhO-Ph-	(2-Ph-ethyl)(Me)N-C(O)-	HO-
S	C-H	4-MeO-Ph-	(4,4-dimethyl pentyl)NHC(O)-	thienyl-O-
O	C-H	4-MeO-Ph-	3-pyridyl	HO-
O	C-H	5-benzofuranyl	4-morpholino-C(O)-	HO-
O	C-H	4-MeO-Ph-	BzO-C(O)-	HO-
O	C-H	5-benzo-	Ph-NH-C(O)-	(1-Ph-ethyl)

		thiazolyl		NH-C(O)-O-
O	C-H	4-MeO-Ph-	Bz-NH-C(O)-	HO-
O	C-H	4-PhO-Ph-	3-Ph-propyl-NH-C(O)-	HO-
O	C-H	4-MeO-Ph-	(2-Ph-ethyl)(Me)N-C(O)-	vinyl
O	C-H	n-dodecyl	BzEtN-C(O)-	HO-
O	C-H	4-MeO-Ph-	(4,4-dimethyl pentyl)NHC(O)-	PhNH-C(O)-O-
N	S	4-morpholino	phenyl	PhNH-C(O)-O-
N	S	2-naphthyl	3-pyridyl	MeNH-C(O)-O-
N	S	3,4-dimethoxy-phenyl	4-morpholino-C(O)-	i-propylNH-C(O)-O-
S	N	4-piperidinyl-butyl	BzO-C(O)-	(4-PhO-Ph)NH-C(O)-O-
S	N	6-benzo-dioxanyl	Ph-NH-C(O)-	thienyl-NH-C(O)-O-
S	N	4-hydroxy-cyclohexyl	2-pyridyl-NH-C(O)-	(4-MeO-Ph)NH-C(O)-O-
C-H	S	4-MeO-Ph-	BzMeN-C(O)-	3-(3-furyl)-butyl
C-H	S	4-MeO-Ph-	3-pyridyl	2-MeS-ethyl
C-H	S	4-MeO-Ph-	4-acetamido-phenyl	4-methyl-pentyl
C-H	S	4-MeO-Ph-	H-	PhNH-C(O)-ethyl
S	C-H	4-MeO-Ph-	4-chlorobenzyl	4-pyrid-3-yl-butyl
S	C-H	4-MeO-Ph-	4-pyridyl	3-hydroxy-butyl
S	C-H	4-MeO-Ph-	H-	PhNH-C(O)-

				methyl
S	C-H	4-MeO-Ph-	HO-C(O)-	2-(pyrid-3-yl-C(O)-NH)-ethyl
N	S	4-MeO-Ph-	phenyl	2-(2-thienyl-thio)ethyl
N	S	4-MeO-Ph-	4-morpholino-C(O)-	PhNH-C(O)-methyl
N	S	4-MeO-Ph-	3-pyridyl	3-MeS-propyl
S	N	4-MeO-Ph-	EtO-C(O)-	2-phenoxyethyl
S	N	4-MeO-Ph-	Ph-NH-C(O)-	3-pyrid-3-yl-propyl
S	N	4-MeO-Ph-	2-pyridyl-NH-C(O)-	iso-butyl

TABLE VIII



Y	R^1	R^{10}	R^{11}
S	4-MeO-Ph-	BzMeN-C(O)-	HO-
S	4-MeO-Ph-	phenyl	HO-
S	4-MeO-Ph-	EtO-C(O)-	HO-
S	4-MeO-Ph-	HO-C(O)-	HO-
S	4-MeO-Ph-	2-pyridyl	HO-
S	4-CF_3O-Ph-	3-pyridyl	H-
S	4-MeO-Ph-	4-morpholino-C(O)-	HO-
S	4-MeO-Ph-	BzO-C(O)-	HO-

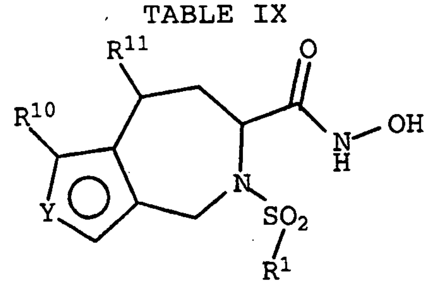
S	4-Me-Ph-	Ph-NH-C(O)-	HO-
S	3-MeO-Ph-	Bz-NH-C(O)-	HO-
S	4-MeO-Ph-	(4,4-dimethyl pentyl)NHC(O)-	HO-
S	4-Cl-Ph-	PhMeN-C(O)-	HO-
S	2-thienyl	PhMeN-C(O)-	HO-
S	4-MeO-Ph-	H-	BzNH-C(O)-O-
S	3,4-dimethoxy-phenyl	H-	PhNH-C(O)-O-
S	4-MeO-Ph-	H-	MeNH-C(O)-O-
S	4-MeO-Ph-	H-	i-propylNH-C(O)-O-
S	4-MeO-Ph-	H-	(4-PhO-Ph)NH-C(O)-O-
S	4-MeO-Ph-	H-	(1-Ph-ethyl) NH-C(O)-O-
S	4-MeO-Ph-	H-	(4-MeO-Ph)NH-C(O)-O-
S	5-benzo-thiazolyl	H-	(2-Ph-ethyl) NH-C(O)-O-
S	phenyl	H-	vinyl-
S	4-CN-Ph-	H-	HO-
S	4-(Me-C(O)-NH)-Ph-	H-	HO-
S	4-i-propyl-Ph-	H-	HO-
S	4-Et-Ph-	H-	HO-
S	4-t-butyl-Ph-	H-	H-
S	n-dodecyl	H-	HO-
S	n-octyl	H-	H-

S	4-MeO-Ph-	Ph-SO_2-NH-	H-
S	4-MeO-Ph-	MeC(O)-NH-	HO-
S	4-MeO-Ph-	MeO-C(O)-NH-	(4-F-Ph)NH-C(O)-O-
O	4-MeO-Ph-	methyl	H-
O	4-MeO-Ph-	Ph-C(O)-NH-	HO-
O	4-MeO-Ph-	H-	benzyl
O	4-MeO-Ph-	H-	HO-
O	4-MeO-Ph-	H-	PhNH-C(O)-O-
O	4-MeO-Ph-	methyl	PhNH-C(O)-O-
O	4-MeO-Ph-	H-	H-
S	4-MeO-Ph-	H-	H-
O	4-MeO-Ph-	EtO-C(O)-	H-
O	4-MeS-Ph-	BzMeN-C(O)-	HO-
O	4-Cl-Ph-	phenyl	Ph-SO_2-NH-
O	4-CF_3O-Ph-	MeO-C(O)-	thienyl-S-
O	5-benzo-dioxolyl	HO-C(O)-	HO-
O	4-Me-Ph-	2-pyridyl	HO-
O	4-MeO-Ph-	3-pyridyl	MeS-
O	4-MeO-Ph-	4-morpholino-C(O)-	HO-
O	n-dodecyl	BzO-C(O)-	HO-
O	4-MeO-Ph-	Ph-NH-C(O)-	thienyl-NH-C(O)-O-
O	furyl	Bz-NH-C(O)-	HO-
O	4-MeO-Ph-	3-Ph-propyl-NH-C(O)-	2-pyridyl-NH-C(O)-O-

S	4-PhO-Ph-	(2-Ph-ethyl) (Me)N-C(O)-	HO-
S	4-pyridyl	BzEtN-C(O)-	propargyl
S	4-MeO-Ph-	(4,4-dimethyl pentyl)NHC(O)-	thienyl-O-
S	5-benzofuranyl	4-morpholino-C(O)-	HO-
S	5-benzo-thiazolyl	Ph-NH-C(O)-	(1-Ph-ethyl) NH-C(O)-O-
S	4-PhO-Ph-	3-Ph-propyl-NH-C(O)-	HO-
S	4-MeO-Ph-	(2-Ph-ethyl) (Me)N-C(O)-	vinyl
S	n-dodecyl	BzEtN-C(O)-	HO-
S	4-MeO-Ph-	(4,4-dimethyl pentyl)NHC(O)-	PhNH-C(O)-O-
S	4-morpholino	phenyl	PhNH-C(O)-O-
S	3,4-dimethoxy-phenyl	4-morpholino-C(O)-	i-propylNH-C(O)-O-
S	4-piperidinyl-butyl	BzO-C(O)-	(4-PhO-Ph)NH-C(O)-O-
S	6-benzo-dioxanyl	Ph-NH-C(O)-	thienyl-NH-C(O)-O-
S	2-naphthyl	3-pyridyl	MeNH-C(O)-O-
S	4-hydroxy-cyclohexyl	2-pyridyl-NH-C(O)-	(4-MeO-Ph)NH-C(O)-O-
S	4-MeO-Ph-	BzMeN-C(O)-	3-(3-furyl)-butyl
S	4-MeO-Ph-	4-acetamido-phenyl	4-methyl-pentyl
S	4-MeO-Ph-	3-pyridyl	2-MeS-ethyl

S	4-MeO-Ph-	H-	PhNH-C(O)-ethyl
O	4-MeO-Ph-	4-chlorobenzyl	4-pyrid-3-yl-butyl
O	4-MeO-Ph-	4-pyridyl	3-hydroxybutyl
O	4-MeO-Ph-	H-	PhNH-C(O)-methyl
O	4-MeO-Ph-	HO-C(O)-	2-(pyrid-3-yl-C(O)-NH)-ethyl
S	4-MeO-Ph-	phenyl	2-(2-thienyl-thio)ethyl
S	4-MeO-Ph-	3-pyridyl	3-MeS-propyl
S	4-MeO-Ph-	4-morpholino-C(O)-	PhNH-C(O)-methyl
S	4-MeO-Ph-	EtO-C(O)-	2-phenoxyethyl
S	4-MeO-Ph-	Ph-NH-C(O)-	3-pyrid-3-yl-propyl
S	4-MeO-Ph-	2-pyridyl-NH-C(O)-	iso-butyl

TABLE IX



Y	R^1	R^{10}	R^{11}
S	4-MeO-Ph-	BzMeN-C(O)-	HO-
S	4-MeO-Ph-	phenyl	HO-
S	4-MeO-Ph-	EtO-C(O)-	HO-
S	4-MeO-Ph-	HO-C(O)-	HO-

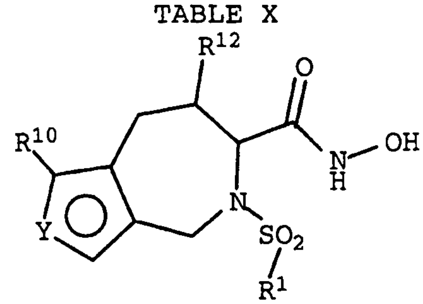
S	4-MeO-Ph-	2-pyridyl	HO-
S	4-CF_3O-Ph-	3-pyridyl	H-
S	4-MeO-Ph-	BzO-C(O)-	HO-
S	4-MeO-Ph-	4-morpholino-C(O)-	HO-
S	4-Me-Ph-	Ph-NH-C(O)-	HO-
S	3-MeO-Ph-	Bz-NH-C(O)-	HO-
S	4-MeO-Ph-	(4,4-dimethyl pentyl)NHC(O)-	HO-
S	4-Cl-Ph-	PhMeN-C(O)-	HO-
S	2-thienyl	PhMeN-C(O)-	HO-
S	4-MeO-Ph-	H-	BzNH-C(O)-O-
S	3,4-dimethoxy-phenyl	H-	PhNH-C(O)-O-
S	4-MeO-Ph-	H-	MeNH-C(O)-O-
S	4-MeO-Ph-	H-	i-propylNH-C(O)-O-
S	4-MeO-Ph-	H-	(4-PhO-Ph)NH-C(O)-O-
S	4-MeO-Ph-	H-	(1-Ph-ethyl) NH-C(O)-O-
S	4-MeO-Ph-	H-	(4-MeO-Ph)NH-C(O)-O-
S	5-benzo-thiazolyl	H-	(2-Ph-ethyl) NH-C(O)-O-
S	phenyl	H-	vinyl-
S	4-CN-Ph-	H-	HO-
S	4-(Me-C(O)-NH)-Ph-	H-	HO-
S	4-i-propyl-Ph-	H-	HO-

S	4-Et-Ph-	H-	HO-
S	4-t-butyl-Ph-	H-	H-
S	n-dodecyl	H-	HO-
S	n-octyl	H-	H-
S	4-MeO-Ph-	Ph-SO_2-NH-	H-
S	4-MeO-Ph-	MeC(O)-NH-	HO-
S	4-MeO-Ph-	MeO-C(O)-NH-	(4-F-Ph)NH-C(O)-O-
O	4-MeO-Ph-	methyl	H-
O	4-MeO-Ph-	Ph-C(O)-NH-	HO-
O	4-MeO-Ph-	H-	benzyl
O	4-MeO-Ph-	H-	HO-
O	4-MeO-Ph-	H-	PhNH-C(O)-O-
O	4-MeO-Ph-	methyl	PhNH-C(O)-O-
O	4-MeO-Ph-	H-	H-
S	4-MeO-Ph-	H-	H-
O	4-MeO-Ph-	EtO-C(O)-	H-
O	4-MeS-Ph-	BzMeN-C(O)-	HO-
O	4-Cl-Ph-	phenyl	Ph-SO_2-NH-
O	4-CF_3O-Ph-	MeO-C(O)-	thienyl-S-
O	5-benzo-dioxolyl	HO-C(O)-	HO-
O	4-Me-Ph-	2-pyridyl	HO-
O	4-MeO-Ph-	3-pyridyl	MeS-
O	4-MeO-Ph-	4-morpholino-C(O)-	HO-
O	n-dodecyl	BzO-C(O)-	HO-
O	4-MeO-Ph-	Ph-NH-C(O)-	thienyl-NH-

			C(O)-O-
O	4-MeO-Ph-	3-Ph-propyl-NH-C(O)-	2-pyridyl-NH-C(O)-O-
O	furyl	Bz-NH-C(O)-	HO-
S	4-PhO-Ph-	(2-Ph-ethyl)(Me)N-C(O)-	HO-
S	4-pyridyl	BzEtN-C(O)-	propargyl
S	4-MeO-Ph-	(4,4-dimethyl pentyl)NHC(O)-	thienyl-O-
S	5-benzofuranyl	4-morpholino-C(O)-	HO-
S	5-benzo-thiazolyl	Ph-NH-C(O)-	(1-Ph-ethyl)NH-C(O)-O-
S	4-PhO-Ph-	3-Ph-propyl-NH-C(O)-	HO-
S	4-MeO-Ph-	(2-Ph-ethyl)(Me)N-C(O)-	vinyl
S	n-dodecyl	BzEtN-C(O)-	HO-
S	4-MeO-Ph-	(4,4-dimethyl pentyl)NHC(O)-	PhNH-C(O)-O-
S	4-morpholino	phenyl	PhNH-C(O)-O-
S	2-naphthyl	3-pyridyl	MeNH-C(O)-O-
S	3,4-dimethoxy-phenyl	4-morpholino-C(O)-	i-propylNH-C(O)-O-
S	4-piperidinyl-butyl	BzO-C(O)-	(4-PhO-Ph)NH-C(O)-O-
S	6-benzo-dioxanyl	Ph-NH-C(O)-	thienyl-NH-C(O)-O-
S	4-hydroxy-cyclohexyl	2-pyridyl-NH-C(O)-	(4-MeO-Ph)NH-C(O)-O-
S	4-MeO-Ph-	BzMeN-C(O)-	3-(3-furyl)-

			butyl
S	4-MeO-Ph-	4-acetamido-phenyl	4-methyl-pentyl
S	4-MeO-Ph-	3-pyridyl	2-MeS-ethyl
S	4-MeO-Ph-	H-	PhNH-C(O)-ethyl
O	4-MeO-Ph-	4-chlorobenzyl	4-pyrid-3-yl-butyl
O	4-MeO-Ph-	4-pyridyl	3-hydroxy-butyl
O	4-MeO-Ph-	H-	PhNH-C(O)-methyl
O	4-MeO-Ph-	HO-C(O)-	2-(pyrid-3-yl-C(O)-NH)-ethyl
S	4-MeO-Ph-	phenyl	2-(2-thienyl-thio)ethyl
S	4-MeO-Ph-	3-pyridyl	3-MeS-propyl
S	4-MeO-Ph-	4-morpholino-C(O)-	PhNH-C(O)-methyl
S	4-MeO-Ph-	EtO-C(O)-	2-phenoxyethyl
S	4-MeO-Ph-	Ph-NH-C(O)-	3-pyrid-3-yl-propyl
S	4-MeO-Ph-	2-pyridyl-NH-C(O)-	iso-butyl

TABLE X



Y	R1	R10	R12
S	4-MeO-Ph-	BzMeN-C(O)-	HO-
S	4-MeO-Ph-	phenyl	HO-
S	4-MeO-Ph-	EtO-C(O)-	HO-
S	4-MeO-Ph-	HO-C(O)-	HO-
S	4-MeO-Ph-	2-pyridyl	HO-
S	4-CF_3O-Ph-	3-pyridyl	H-
S	4-MeO-Ph-	4-morpholino-C(O)-	HO-
S	4-MeO-Ph-	BzO-C(O)-	HO-
S	4-Me-Ph-	Ph-NH-C(O)-	HO-
S	3-MeO-Ph-	Bz-NH-C(O)-	HO-
S	4-MeO-Ph-	(4,4-dimethyl pentyl)NHC(O)-	HO-
S	4-Cl-Ph-	PhMeN-C(O)-	HO-
S	2-thienyl	PhMeN-C(O)-	HO-
S	3,4-dimethoxy-phenyl	H-	PhNH-C(O)-O-
S	4-MeO-Ph-	H-	BzNH-C(O)-O-
S	4-MeO-Ph-	H-	i-propylNH-C(O)-O-
S	4-MeO-Ph-	H-	(4-PhO-Ph)NH-C(O)-O-
S	4-MeO-Ph-	H-	MeNH-C(O)-O-
S	4-MeO-Ph-	H-	(1-Ph-ethyl) NH-C(O)-O-
S	4-MeO-Ph-	H-	(4-MeO-Ph)NH-C(O)-O-
S	5-benzo-	H-	(2-Ph-ethyl)

	thiazolyl		NH-C(O)-O-
S	phenyl	H-	vinyl-
S	4-CN-Ph-	H-	HO-
S	4-(Me-C(O)-NH)-Ph-	H-	HO-
S	4-i-propyl-Ph-	H-	HO-
S	4-Et-Ph-	H-	HO-
S	4-t-butyl-Ph-	H-	H-
S	n-dodecyl	H-	HO-
S	n-octyl	H-	H-
S	4-MeO-Ph-	Ph-SO_2-NH-	H-
S	4-MeO-Ph-	MeC(O)-NH-	HO-
S	4-MeO-Ph-	MeO-C(O)-NH-	(4-F-Ph)NH-C(O)-O-
O	4-MeO-Ph-	methyl	H-
O	4-MeO-Ph-	Ph-C(O)-NH-	HO-
O	4-MeO-Ph-	H-	benzyl
O	4-MeO-Ph-	H-	HO-
O	4-MeO-Ph-	H-	PhNH-C(O)-O-
O	4-MeO-Ph-	methyl	PhNH-C(O)-O-
O	4-MeO-Ph-	H-	H-
S	4-MeO-Ph-	H-	H-
O	4-MeO-Ph-	EtO-C(O)-	H-
O	4-MeS-Ph-	BzMeN-C(O)-	HO-
O	4-Cl-Ph-	phenyl	Ph-SO_2-NH-
O	4-CF_3O-Ph-	MeO-C(O)-	thienyl-S-
O	5-benzo-dioxolyl	HO-C(O)-	HO-

O	4-Me-Ph-	2-pyridyl	HO-
O	4-MeO-Ph-	3-pyridyl	MeS-
O	4-MeO-Ph-	4-morpholino-C(O)-	HO-
O	4-MeO-Ph-	Ph-NH-C(O)-	thienyl-NH-C(O)-O-
O	n-dodecyl	BzO-C(O)-	HO-
O	furyl	Bz-NH-C(O)-	HO-
O	4-MeO-Ph-	3-Ph-propyl-NH-C(O)-	2-pyridyl-NH-C(O)-O-
S	4-PhO-Ph-	(2-Ph-ethyl)(Me)N-C(O)-	HO-
S	4-pyridyl	BzEtN-C(O)-	propargyl
S	4-MeO-Ph-	(4,4-dimethyl pentyl)NHC(O)-	thienyl-O-
S	5-benzofuranyl	4-morpholino-C(O)-	HO-
S	5-benzo-thiazolyl	Ph-NH-C(O)-	(1-Ph-ethyl)NH-C(O)-O-
S	4-PhO-Ph-	3-Ph-propyl-NH-C(O)-	HO-
S	4-MeO-Ph-	(2-Ph-ethyl)(Me)N-C(O)-	vinyl
S	4-MeO-Ph-	(4,4-dimethyl pentyl)NHC(O)-	PhNH-C(O)-O-
S	n-dodecyl	BzEtN-C(O)-	HO-
S	4-morpholino	phenyl	PhNH-C(O)-O-
S	2-naphthyl	3-pyridyl	MeNH-C(O)-O-
S	3,4-dimethoxy-phenyl	4-morpholino-C(O)-	i-propylNH-C(O)-O-

S	4-piperidinyl-butyl	BzO-C(O)-	(4-PhO-Ph)NH-C(O)-O-
S	6-benzo-dioxanyl	Ph-NH-C(O)-	thienyl-NH-C(O)-O-
S	4-hydroxy-cyclohexyl	2-pyridyl-NH-C(O)-	(4-MeO-Ph)NH-C(O)-O-
S	4-MeO-Ph-	3-pyridyl	2-MeS-ethyl
S	4-MeO-Ph-	BzMeN-C(O)-	3-(3-furyl)-butyl
S	4-MeO-Ph-	4-acetamido-phenyl	4-methyl-pentyl
S	4-MeO-Ph-	H-	PhNH-C(O)-ethyl
O	4-MeO-Ph-	4-chlorobenzyl	4-pyrid-3-yl-butyl
O	4-MeO-Ph-	4-pyridyl	3-hydroxybutyl
O	4-MeO-Ph-	H-	PhNH-C(O)-methyl
O	4-MeO-Ph-	HO-C(O)-	2-(pyrid-3-yl-C(O)-NH)-ethyl
S	4-MeO-Ph-	phenyl	2-(2-thienyl-thio)ethyl
S	4-MeO-Ph-	3-pyridyl	3-MeS-propyl
S	4-MeO-Ph-	4-morpholino-C(O)-	PhNH-C(O)-methyl
S	4-MeO-Ph-	EtO-C(O)-	2-phenoxyethyl
S	4-MeO-Ph-	Ph-NH-C(O)-	3-pyrid-3-yl-propyl
S	4-MeO-Ph-	2-pyridyl-NH-C(O)-	iso-butyl

Example 73

The following assays are in vitro assays which were used to characterize the ability of compounds of this invention to inhibit the production of TNF-α by monocytes following LPS stimulation, Human Monocyte TNF Convertase Assay, Human Neutrophil Collagenase Assay and Human Fibroblast Stromelysin Assay.

Lipopolysaccharide-activated monocyte TNF production assay

Isolation of monocytes

Test compounds were evaluated *in vitro* for the ability to inhibit the production of tumor necrosis factor (TNF) by monocytes activated with bacterial lipopolysaccharide (LPS). Fresh residual source leukocytes (a byproduct of plateletpheresis) were obtained from the local blood bank and peripheral blood mononuclear cells (PBMCs) were isolated by density gradient centrifugation on Ficol-Paque Plus (Pharmacia). PBMCs were suspended at 2 x 10^6/ml in DMEM supplemented to contain 2% FCS (10 mM), 0.3 mg/ml glutamate, 100 U/ml penicillin G and 100 mg/ml streptomycin sulfate (complete media). Cells were plated into Falcon flatbottom 96 well culture plates (200 µl/well) and cultured overnight at 37°C and 6% CO_2. Nonadherent cells were removed by washing with 200 µl/well of fresh medium. Wells containing adherent cells (~70% monocytes) were replenished with 100 µl of fresh medium.

Preparation of test compound stock solutions

Test compounds were dissolved in DMS. Compound stock solutions were prepared to an initial concentration of 10 - 50 µM. Stocks were diluted initially to 20 - 200 µM in complete media. Nine two-fold serial dilutions of each compound were then prepared in complete medium.

Treatment of cells with test compounds and activation of TNF production with lipopolysaccharide

One hundred microliters of each test compound dilution were added to microtiter wells containing adherent monocytes and 100 µl complete medium. Monocytes were cultured with test compounds for 60 min at which time 25 µl of complete medium containing 30 ng/ml lipopolysaccharide from *E. coli* K532 were added to each well. Cells were cultured an additional 4 hrs. Culture supernatants were then removed and TNF present in the supernatants was quantified using an ELISA.

TNF ELISA

Flat bottom 96 well Corning High Binding ELISA plates were coated overnight (4^{o}C) with 150 µL/well of 3 µg/ml murine anti-human TNFa MAb (R&D Systems #MAB210). Wells were then blocked 1 h at room temperature with 200 µL/well of $CaCl_2$-free ELISA buffer supplemented to contain 20 mg/ml BSA (standard ELISA buffer: 20 mM, 150 mM NaCl, 2 mM $CaCl_2$, 0.15 mM thimerosal, pH 7.4). Plates were washed and replenished with 100 µl of test supernatants (diluted 1:3) or standards. Standards consisted of eleven 1.5-fold serial dilutions from a stock of 1 ng/ml recombinant human TNF (R&D Systems). Plates were incubated at room temperature for 1 h on orbital shaker (300 rpm), washed and replenished with 100 µl/well of 0.5 µg/ml goat anti-human TNFa (R&D systems #AB-210-NA) biotinylated at a 4:1 ratio. Plates were incubate for 40 min, washed and replenished with 100 µl/well of alkaline phosphatase-conjugated streptavidin (Jackson ImmunoResearch #016-050-084) at 0.02 µg/ml. Plates were incubated 30 min, washed and replenished with 200 µl/well of 1 mg/ml of p-nitrophenyl phosphate. After 30 min, plates were read at 405 nm on a Vmax plate reader.

Data analysis

Standard curve data were fit to a second order polynomial and unknown TNFa concentrations determined from their OD by solving this equation for concentration. TNF concentrations were then plotted vs. test compound concentration using a second order polynomial. This equation was then used to calculate the concentration of test compounds causing a 50% reduction in TNF production.

Human Monocyte TNF Convertase Assay

TNF convertase activity is demonstrated by hydrolytic cleavage of a dinitrophenyl (DNP)-labeled peptide substrate between amino acids Ala and Val. Dependent on the purity of the TNF convertase used in the reaction, hydrolysis of incorrectly clipped DNP-peptides are also possible. Human monocyte TNF convertase activity is determined by using DNP-labeled peptide substrate (1) Dnp-SPLAQAVRSSSR-CONH2; and clipped peptides: (2) DNP-SPLAQ-COOH (incorrectly clipped between Gln and Ala); (3) DNP-SPLAQA-COOH (correctly clipped); and (4) DNP-SPLAQAV-COOH (incorrectly clipped between Val and Arg).

Full length and clipped DNP-peptides are separated and quantitated using reversed phase HPLC, monitoring at 350 nM (where dinitrophenyl absorbs). Inhibitors of TNF convertase in the reaction are detected by a decrease in peak height of peptide 3 and an increase in peak height of peptide 1. Inhibition is calculated as percent of control by comparing peak height of peptide 3 in samples with no inhibitors (control conditions) and peak height of peptide no. 3 in samples with inhibitors.

Typically, compounds at 2 mM in DMSO are first diluted 1:11.8 in 40 mM Tris, pH 7.5. A further 1:17 dilution of the compound occurs in the final reaction mixture. This reaction mixture contains 2.5μL of the

diluted compound, 20 μL of peptide 1, and 20 μL of TNF convertase. This results in a compound concentration of 10 μM, 0.5% DMSO, in the final reaction volume. Compounds are initially screened at 10 uM and selected compounds are further assayed to determine an IC_{50}.

Human Neutrophil Collagenase Assay

Human neutrophil collagenase (HNC) activity is determined by using fluorogenic peptide substrate Dnp-Pro-b-Cyclohexyl-Ala-Gly-Cys(Me)-His-Ala-Lys-(N-methylanthranilic acid)-NH_2. The N-terminus Dnp group and the C-terminus N-methyl-anthranilyl moiety (Nma) are fluorescence self-quenching until the peptide is cleaved at the Gly-Cys(me) bond. The fluorescence from the cleavage products is measured on a Bio-Tek Instrument FL500 fluorescence micro-plate reader (excitation at 360 nm, emission at 460 nm). The assay is performed in a 96-well plate (in duplicate), and the Km = 51 nM for the substrate, and Ki = 722 nM for Actinonin have been determined. The test compounds (at 100, 33 & 10 mM) are compared for their inhibition of HNC activity on the substrate against the activity of Actinonin and Ki's were determined on selected compounds.

Human Fibroblast Stromelysin Assay

Human fibroblast stromelysin (HFS) activity is determined by using fluorogenic peptide substrate Dnp-Pro-b-Cyclohexyl-Ala-Gly-Cys(Me)-His-Ala-Lys-(N-methylanthranilic acid)-NH_2. The N-terminus Dnp group and the C-terminus N-methyl-anthranilyl moiety (Nma) are fluorescence self-quenching until the peptide is cleaved at the Gly-Cys(me) bond. The fluorescence from the cleavage products is measured on a Bio-Tek Instrument FL500 fluorescence micro-plate reader (excitation at 360 nm, emission at 460 nm). The assay is performed in a 96-well plate (in duplicate), and the Km = 51 nM for the substrate, and Ki = 722 nM for Actinonin (an inhibitor

of enzyme activity; Sigma Chemical, St. Louis, MO; A6671) have been determined as the standard control. The test compounds (at 100, 33 & 10 mM) are compared for their inhibition of HFS activity on the substrate against the activity of Actinonin and Ki's were determined on selected compounds.

Inhibition of LPS-Induced TNF-α production in mice

Male DBA/1LACJ mice were dosed with vehicle or test compounds in a vehicle (the vehicle consisting of 0.5% tragacanth in 0.03 N HCl) prior to lipopolysaccharide (2 mg/kg, I.V.) injection. Ninety minutes after LPS injection, blood was collected and the serum was analyzed by ELISA for TNF levels.

The following compounds had a TNF convertase, HNC and/or HFS inhibition activity IC_{50} of less than 1μM:

4-cis-hydroxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid

4-trans-hydroxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid

4-cis-vinyl-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid

4-cis-hydroxymethyl-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid

4-trans-benzyl-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid

6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-hydroxamic acid

4-oxo-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-hydroxamic acid

4-cis-hydroxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-hydroxamic acid

4-cis-methoxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-hydroxamic acid

5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-trans-hydroxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-methyl-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

5-(4-methoxyphenylsulfonyl)-2-carboxy-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-carboxy-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

5-(4-methoxyphenylsulfonyl)-2-(methoxycarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(methoxycarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(ethoxycarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-pyrid-2-yl-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-pyrid-3-yl-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-phenyl-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-phenylaminocarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-(phenylmethyl)aminocarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-phenylmethyl-N-methylaminocarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-(3-phenylpropyl)aminocarbonyl)-4,5,6,7-tetrahydrothien[3,2-c]pyridine-6-hydroxamic acid

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-(4,4-diphenylbutyl)aminocarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-(3,3-dimethylbutyl)aminocarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(aminocarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(morpholinocarbonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

4-benzyl-8-cis-hydroxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid

4-cis-benzyl-8-cis-hydroxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid

4-trans-benzyl-8-hydroxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3,d]azepine-5-hydroxamic acid

4-trans-benzyl-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid

4-trans-benzyl-6-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[2,3,-c]pyridine-5-hydroxamic acid

7-cis-(aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-(N-methylaminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-(N-prop-2-ylaminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-(N-cyclohexylaminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-(N-phenylaminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-(N-(4-methoxyphenyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-(N-(4-phenoxyphenyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-(N-(2-biphenyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-(N-(phenylmethyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-(N-(1(S)-phenylethyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-(N-(2-phenylethyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-(N-(3-methoxyphenyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-(N-(2-methoxyphenyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-(N-(2-chlorophenyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-(N-(3-chlorophenyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-(N-(4-chlorophenyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-(N-(4-fluorophenyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-(N-(4-cyanophenyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-(N-(4-butoxycarbonylphenyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-(N-(4-tolyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-(N-(3-tolyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

7-cis-(N-(1-naphthyl)aminocarbonyl)oxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno[3,2-c]pyridine-6-hydroxamic acid

trans-(+/-)-7-(4-methoxyphenylsulfonyl)-5-phenethyl-4,5,6,7,8,9-hexahydrothieno[2,3-*d*]azocine-6-hydroxamic acid

trans-(+/-)-6-(4-methoxyphenylsulfonyl)-4-vinyl-4,5,6,7-tetrahydrothieno[2,3-*c*]pyridine-5-hydroxamic acid

trans-(+/-)-6-(4-methoxyphenylsulfonyl)-4-phenethyl-5,6,7,8-tetrahydro-4*H*-thieno[2,3-*d*]azepine-5-hydroxamic acid

Selected compounds from this invention have demonstrated antiinflammatory properties in a adjuvant arthritis model. Also, selected compounds from the class have shown in vivo activity in a LPS mouse model in which serum levels of TNF-α were reduced in the presence of compounds of this invention.

Methods of Treatment

All of the compounds of this invention are useful in the prophylaxis and treatment of TNF-α mediated disease states. The compounds are also useful in the prophylaxis and treatment of disease states in which HNC and/or HFS play a role. Preferably, the compounds of this invention are useful in the prophylaxis and treatment of rheumatoid arthritis; osteoarthritis; rheumatoid spondylitis; gouty arthritis; inflammatory bowel disease; adult respiratory distress syndrome (ARDS); psoriasis; Crohn's disease; allergic rhinitis;

ulcerative colitis; anaphylaxis; contact dermatitis; asthma; antiviral therapy including those viruses sensitive to TNF-α inhibition - HIV-1, HIV-2, HIV-3, cytomegalovirus (CMV), influenza, adenovirus, and the herpes viruses including HSV-1, HSV-2, and herpes zoster; muscle degeneration; cachexia; Reiter's syndrome; type II diabetes; bone resorption diseases; graft vs. host reaction; ischemia reperfusion injury; brain trauma; atherosclerosis; Alzheimer's discease; multiple sclerosis; cerebral malaria; sepsis; septic shock; toxic shock syndrome; fever and mylagias due to infection.

The present invention provides a method of treating a disease state in which TNF-α, HNC and/or HFS levels are elevated which comprises administering an effective amount of a compound of this invention. Compounds of this invention are of use in the prophylaxis and acute or chronic therapy of any disease state in a human, or other mammal, which is exacerbated by or mediated by elevated or unregulated TNF-α, HNC and/or HFS by mammal's cells. More preferably, this invention relates to a method of lowering the levels of TNF-α in a mammal in need thereof which comprises administering an effective dose of a compound of this invention or a pharmaceutical composition thereof. In addition, this invention relates to a method of lowering the activity levels of HNC and/or HFS in a mammal in need thereof which comprises administering an effective dose of a compound of this invention or a pharmaceutical composition thereof.

A compound of this invention or a pharmaceutical composition thereof is useful in the treatment or prophylaxis of a number of disease states including rheumatoid arthritis; osteoarthritis; rheumatoid spondylitis; gouty arthritis; inflammatory bowel disease; adult respiratory distress syndrome (ARDS);

psoriasis; Crohn's disease; allergic rhinitis; ulcerative colitis; anaphylaxis; contact dermatitis; asthma; antiviral therapy including those viruses sensitive to TNF-α inhibition - HIV-1, HIV-2, HIV-3, cytomegalovirus (CMV), influenza, adenovirus, and the herpes viuses including HSV-1, HSV-2, and herpes zoster; muscle degeneration; cachexia; Reiter's syndrome; type II diabetes; bone resorption diseases; graft vs. host reaction; ischemia reperfusion injury; atherosclerosis; brain trauma; Alzheimer's disease; multiple sclerosis; cerebral malaria; sepsis; septic shock; toxic shock syndrome; fever and mylagias due to infection.

Pharmaceutical Compositions

This invention further relates to the use of a compound of this invention in the manufacture of a medicament for the prophylaxis and treatment, either acutely or chronically, of TNF-α mediated disease states. In addition, the compounds of this invention are useful in the manufacture of a medicament for treating disease states in which HNC and/or HFS play a role.

This invention also relates to a pharmaceutical composition comprising a compound of this invention and a pharmaceutically acceptable carrier, and if desired other active ingredients. The compounds of this invention are administered by any suitable route, preferably in the form of a pharmaceutical composition adapted to such a route, and in a dose effective for the treatment intended. Therapeutically effective doses of the compounds of the present invention required to arrest the progress or prevent tissue damage associated with the disease are readily ascertained by one of ordinary skill in the art.

For the prophylaxis and treatment of disease states, the compounds of the present invention may be administered orally, parentally, or by inhalation spray,

rectally, or topically in dosage unit formulations containing conventional pharmaceutically acceptable carriers, adjuvants and vehicles. The term parenteral as used herein includes, subcutaneous, intravenous, intramuscular, intrasternal, infusion techniques or intraperitoneally.

The amount of active ingredient that may be combined with the carrier materials to produce a single dosage form will vary depending upon the host treated and the particular mode of administration.

The dosage regimen for treating a disease state with the compounds of this invention and/or compositions of this invention is based on a variety of factors, including the type of disease, the age, weight, sex and medical condition of the patient, the severity of the condition, the route of administration, pharmacological considerations such as the activity, efficacy, pharmacokinetic and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized and whether the compound is administered as part of a drug combination. Thus the dosage regimen may vary widely. Dosage levels of the order from about 0.01 mg to 80 mg per kilogram of body weight per day, preferably from about 0.5 mg to 30 mg/kg, more preferably from about 1 mg to 15 mg/kg are useful for all methods of use disclosed herein. The pharmaceutically active compounds of this invention can be processed in accordance with convential methods of pharmacy to produce medicinal agents for administration to patients, mammals including humans.

For oral administration, the pharmaceutical composition may be in the form of, for example, a capsule, a tablet, a suspension, or liquid. The pharmaceutical composition is preferably made in the form of a dosage unit containing a given amount of the active ingredient. For example, these may contain an amount of active ingredient from about 1 to 250 mg,

preferably from about 25 to 150 mg. A suitable daily dose for a human or other mammal may vary widely depending on the condition of the patient and other factors.

The compounds of this invention may also be administered by injection as a composition with suitable carriers including saline, dextrose, or water. The daily parenteral dosage regimen wll be from about 0.1 to about 80 mg/kg of total body weight, preferably from about 0.5 to about 30 mg/kg, and more preferably from about 1 mg to 15 mg/kg.

Injectable preparations, for example, sterile injectable aqueous or oleaginous suspensions may be formulated according to the known art using suitable dispersing or wetting agents and suspending agents. The sterile injectable preparation may also be a sterile injectable solution or suspension in a nontoxic parenterally acceptable diluent or solvent, for example, as a solution in 1,3-butanediol. Among the acceptable vehicles and solvents that may be employed are water, Ringer's solution, and isotonic sodium chloride solution. In addition, sterile, fixed oils are conventionally employed as a solvent or suspending medium. For this purpose any bland fixed oil may be employed including synthetic mono- or diglycerides. In addition, fatty acids such as oleic acid find use in the preparation of injectables.

Suppositories for rectal administration of the drug can be prepared by mixing the drug with a suitable nonirritating excipient such as cocoa butter and polyethylene glycols which are solid at ordinary temperatures but liquid at the rectal temperature and will therefore melt in the rectum and release the drug.

A suitable topical dose of compounds of this invention is 0.1 mg to 150 mg administered one to four, preferably two or three times daily. For topical administration, the active ingredient may comprise from

0.001% to 10% w/w, e.g. from 1% to 2% by weight of the formulation, although it may comprise as much as 10% w/w, but preferably not more than 5% w/w, and more preferably from 0.1% to 1% of the formulation. Formulations suitable for topical administration include liquid or semi-liquid peparations suitable for penetration through the skin such as liniments, lotions, ointments, creams, or pastes and drops suitable for administration to the eye, ear, or nose.

For administration, the compounds of this invention are ordinarily combined with one or more adjuvants appropriate for the indicated route of administration. The compounds may be admixed with lactose, sucrose, starch powder, cellulose esters of alkanoic acids, stearic acid, talc, magnesium stearate, sodium, magnesium oxide, sodium and calcium salts of phosphoric and sulphuric acids, acacia, gelatin, sodium alginate, polyvinylpyrrolidine, and/or polyvinyl alcohol, and tableted or encapsulated for conventional administration. Alternatively, the compounds of this invention may be dissolved in saline, water, polyethylene glycol, propylene glycol, ethanol, corn oil, peanut oil, cottonseed oil, sesame oil, benzyl alcohol, and/or various buffers. Other adjuvants and modes of administration are well known in the pharmaceutical art. The carrier or diluent may include time delay material, such as glyceryl monostearate or glyceryl distearate alone or with a wax, or other materials well known in the art.

The pharmaceutical compositions may be made up in a solid form including granules, powders or suppositories or in a liquid form such as solutions, suspensions, or emulsions. The pharmaceutical compositions may be subjected to conventional pharmaceutical operations such as sterilization and/or may contain conventional adjuvants, such as preservatives, stabilizers, wetting agents, emulsifiers, buffers, etc.

Solid dosage forms for oral administration may include capsules, tablets, pills, powders, and granules. In such solid dosage forms, the active compound may be admixed with at least one inert diluent such as sucrose lactose or starch. Such dosage forms may also comprise, as in normal practice, additional substances other than inert diluents, e.g., lubricating agents such as magnesium stearate. In the case of capsules, tablets, and pills, the dosage forms may also comprise buffering agents. Tablets and pills can additionally be prepared with enteric coatings.

Liquid dosage forms for oral administration may include pharmaceutically acceptable emulsions, solutions, suspensions, syrups, and elixirs containing inert diluents commonly used in the art, such as water. Such compositions may also comprise adjuvants, such as wetting agents, emulsifying and suspending agents, and sweetening, flavoring, and perfuming agents.

Compounds of the present invention can possess one or more asymmetric carbon atoms and are thus capable of existing in the form of optical isomers as well as in the form of racemic or nonracemic mixtures thereof. The optical isomers can be obtained by resolution of the racemic mixtures according to conventional processes, for example by formation of diastereoisomeric salts by treatment with an optically active acid or base. Examples of appropriate acids are tartaric, diacetyltartaric, dibenzoyltartaric, ditoluoyltartaric and camphorsulfonic acid and then separation of the mixture of diastereoisomers by crystallization followed by liberation of the optically active bases from these salts. A different process for separation of optical isomers involves the use of a chiral chromatography column optimally chosen to maximize the separation of the enantiomers. Still another available method involves synthesis of covalent diastereoisomeric molecules by reacting compounds of Formula I with an

optically pure acid in an activated form or an optically pure isocyanate. The synthesized diastereoisomers can be separated by conventional means such as chromatography, distillation, crystallization or sublimation, and then hydrolyzed to deliver the enantiomerically pure compound. The optically active compounds of Formula I can likewise be obtained by utilizing optically active starting materials. These isomers may be in the form of a free acid, a free base, an ester or a salt.

The compounds of the present invention can be used in the form of salts derived from inorganic or organic acids. These salts include but are not limited to the following: acetate, adipate, alginate, citrate, aspartate, benzoate, benzenesulfonate, bisulfate, butyrate, camphorate, camphorsulfonate, digluconate, cyclopentanepropionate, dodecylsulfate, ethanesulfonate, glucoheptanoate, glycerophosphate, hemisulfate, heptanoate, hexanoate, fumarate, hydrochloride, hydrobromide, hydroiodide, 2-hydroxy-ethanesulfonate, lactate, maleate, methanesulfonate, nicotinate, 2-naphthalenesulfonate, oxalate, palmoate, pectinate, persulfate, 3-phenylpropionate, picrate, pivalate, propionate, succinate, tartrate, thiocyanate, tosylate, mesylate and undecanoate. Also, the basic nitrogen-containing groups can be quaternized with such agents as lower alkyl halides, such as methyl, ethyl, propyl, and butyl chloride, bromides, and iodides; dialkyl sulfates like dimethyl, diethyl, dibutyl, and diamyl sulfates, long chain halides such as decyl, lauryl, myristyl and stearyl chlorides, bromides and iodides, aralkyl halides like benzyl and phenethyl bromides, and others. Water or oil-soluble or dispersible products are thereby obtained.

Examples of acids which may be employed to form pharmaceutically acceptable acid addition salts include such inorganic acids as hydrochloric acid, sulphuric

acid and phosphoric acid and such organic acids as oxalic acid, maleic acid, succinic acid and citric acid. Other examples include salts with alkali metals or alkaline earth metals, such as sodium, potassium, calcium or magnesium or with organic bases.

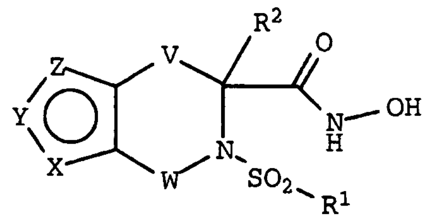
While the compounds of the invention can be administered as the sole active pharmaceutical agent, they can also be used in combination with one or more other agents. When administered as a combination, the therapeutic agents can be formulated as separate compositions which are given at the same time or different times, or the therapeutic agents can be given as a single composition.

The foregoing is merely illustrative of the invention and is not intended to limit the invention to the disclosed compounds. Variations and changes which are obvious to one skilled in the art are intended to be within the scope and nature of the invention which are defined in the appended claims.

From the foregoing description, one skilled in the art can easily ascertain the essential characteristics of this invention, and without departing from the spirit and scope thereof, can make various changes and modifications of the invention to adapt it to various usages and conditions.

WHAT IS CLAIMED IS:

1. A compound of formula



or a pharmacutically acceptable salt thereof, wherein

R^1 is (1) an alkyl, alkenyl, alkynyl, cycloalkyl or heterocyclyl radical optionally substituted by 1-3 radicals of -OH, $-OR^3$, $-SR^3$, $-S(O)R^3$, $-S(O)_2R^3$, $-C(O)R^3$ or $-NR^3R^4$, aryl, heteroaryl, cycloalkyl or heterocyclyl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl, cycloalkyl and heterocyclyl radicals are optionally substituted by 1-3 radicals of hydroxy, $-OR^3$, $-SR^3$, $-S(O)R^3$, $-S(O)_2R^3$, $-C(O)R^3$, $-NR^3R^4$, amino, alkanoylamino, alkylsulfonylamino, alkoxycarbonylamino, alkoxycarbonyl, cyano, halo, azido, alkyl or haloalkyl; provided that the total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^1 is 0-3;

wherein each R^3 is independently an alkyl, haloalkyl, aryl, heteroaryl, aryl-alkyl or heteroaryl-alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, alkoxy, alkylthiol, amino, alkanoylamino, alkylsulfonylamino, alkylsulfinyl, alkylsulfonyl, alkoxycarbonylamino, alkoxycarbonyl, cyano, halo, azido, alkyl, haloalkyl or haloalkoxy; and each R^4 is independently a hydrogen or alkyl radical;

R^2 is a hydrogen or alkyl radical;

V is $-CHR^{11}-$ or $-CHR^{11}-CHR^{12}-$; wherein R^{11} and R^{12} are each independently (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an alkyl, alkenyl or alkynyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, alkoxy, aryloxy, heteroaryloxy, alkylthiol, amino, alkanoylamino, alkylsulfonylamino, alkoxycarbonylamino, alkoxycarbonyl, cyano, halo, azido, alkyl, haloalkyl or haloalkoxy;

wherein each R^{20} is independently a hydrogen, $-C(O)R^{22}$, alkyl, alkenyl, cycloalkyl, aryl, heteroaryl, aryl-alkyl, heteroaryl-alkyl, alkanoyl, aroyl or heteroaroyl radical; wherein the alkyl and alkenyl radicals are optionally substituted by $-C(O)R^{22}$; and wherein the cycloalkyl, aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, alkoxy, alkylthiol, amino, alkanoylamino, alkylsulfonylamino, alkylsulfinyl, alkylsulfonyl, alkoxycarbonylamino, alkoxycarbonyl, cyano, halo, azido, alkyl, haloalkyl or haloalkoxy; and

each R^{21} is independently an alkyl, alkyl-$C(O)R^{22}$, aryl, heteroaryl, aryl-alkyl or heteroaryl-alkyl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, alkoxy, alkylthiol, amino, alkanoylamino, alkylsulfonylamino, alkylsulfinyl, alkylsulfonyl, alkoxycarbonylamino,

alkoxycarbonyl, cyano, halo, azido, alkyl, haloalkyl or haloalkoxy;

wherein each R^{22} is independently a hydroxy, alkoxy, aryloxy, aryl-alkoxy, heteroaryloxy, heteroaryl-alkoxy or $-NR^{23}R^{24}$ radical; wherein R^{23} is a hydrogen, alkyl, aryl, aryl-alkyl, heteroaryl or heteroaryl-alkyl radical; and R^{24} is a hydrogen or alkyl radical; or $-NR^{23}R^{24}$ represents a heterocyclyl or heteroaryl radical; wherein the heterocyclyl, aryl and heteroaryl radicals of R^{22}, R^{23} and $-NR^{23}R^{24}$ are optionally substituted by 1-3 radicals of hydroxy, alkoxy, alkylthiol, amino, alkanoylamino, alkylsulfonylamino, alkylsulfinyl, alkylsulfonyl, alkoxycarbonylamino, alkoxycarbonyl, cyano, halo, azido, alkyl, haloalkyl or haloalkoxy; and

W-N represents -C(O)-N, $-C(O)-CR^{15}R^{16}-N$, $-CR^{15}R^{16}-N$ or $-CR^{17}R^{18}-CR^{15}R^{16}-N$; wherein R^{15} and R^{16} are each independently (1) a hydrogen, $-C(O)R^{22}$, aryl or heteroaryl radical; or (2) an alkyl, alkenyl or alkynyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, alkoxy, alkylthiol, amino, alkanoylamino, alkylsulfonylamino, alkylsulfinyl, alkylsulfonyl, alkoxycarbonylamino, alkoxycarbonyl, cyano, halo, azido, alkyl, haloalkyl or haloalkoxy; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-3; and

R^{17} and R^{18} are each independently (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-$

$C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an alkyl, alkenyl or alkynyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, alkoxy, alkylthiol, amino, alkanoylamino, alkylsulfonylamino, alkylsulfinyl, alkylsulfonyl, alkoxycarbonylamino, alkoxycarbonyl, cyano, halo, azido, alkyl, haloalkyl or haloalkoxy; or one of $-CR^{15}R^{16}-$ or $-CR^{17}R^{18}-$ represent a cycloalkylene or heterocyclylene radical; and

X is O or S, Y is CR^9 and Z is N or CR^{10}; or
Y is O or S, X is CR^8 and Z is CR^{10}; or
Z is O or S, X is N or CR^8 and Y is CR^9;

provided that when W-N represents $-CR^{15}R^{16}-N$ or $-CR^{17}R^{18}-CR^{15}R^{16}-N$, and X is S and Z is CR^{10}, then at least one of R^{11}, R^{12}, R^{15}, R^{16}, R^{17} or R^{18} is other than a hydrogen radical; and provided that when X is O or S and Y and Z are CH, or when Z is O or S and X and Y are CH, then R^{15} is other than a hydrogen or hydroxy radical or at least one of R^{11}, R^{12}, R^{16}, R^{17} or R^{18} is other than a hydrogen radical;

wherein R^8, R^9 and R^{10} are each independently -B-A, provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^8, R^9 and R^{10} is 0-3;

wherein each B is independently a

(1) bond;

(2) alkyl, alkenyl or alkynyl radical optionally substituted by (a) 1-3 radicals of amino, alkylamino, dialkylamino, alkanoylamino, alkoxycarbonylamino, alkylsulfonylamino, hydroxy, alkoxy, alkylthio, cyano or halo, and/or (b) 1-2 radicals of heterocyclyl, aryl or heteroaryl optionally substituted by 1-3 radicals of amino, alkylamino, dialkylamino, alkanoylamino, alkoxycarbonylamino, alkylsulfonylamino, hydroxy, alkoxy, alkylthio, cyano, halo, alkyl, haloalkyl or haloalkoxy;

(3) heterocyclyl radical optionally substituted by 1-3 radicals of amino, alkylamino, dialkylamino, alkanoylamino, alkoxycarbonylamino, alkylsulfonylamino, hydroxy, alkoxy, alkylthio, cyano, alkyl, haloalkyl or haloalkoxy; or

(4) aryl or heteroaryl radical optionally substituted by 1-3 radicals of amino, alkylamino, dialkylamino, alkanoylamino, alkoxycarbonylamino, alkylsulfonylamino, hydroxy, alkoxy, alkylthio, cyano, halo, alkyl, haloalkyl or haloalkoxy;

each A is independently a

(1) hydrogen radical;

(2) halo, cyano or nitro radical;

(3) $-C(O)-R^{30}$, $-C(O)-OR^{31}$, $-C(O)-NR^{32}R^{31}$ or $-C(NR^{32})-NR^{32}R^{31}$ radical;

(4) $-OR^{31}$, $-O-C(O)-R^{31}$, $-O-C(O)-NR^{32}R^{31}$ or $-O-C(O)-NR^{33}-S(O)_2-R^{30}$ radical;

(5) $-SR^{31}$, $-S(O)-R^{30}$, $-S(O)_2-R^{30}$, $-S(O)_2-NR^{32}R^{31}$, $-S(O)_2-NR^{33}-C(O)-R^{31}$, $-S(O)_2-NR^{33}-C(O)-OR^{30}$ or $-S(O)_2-NR^{33}-C(O)-NR^{32}R^{31}$ radical; or

(6) $-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(NR^{32})-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$ or $-NR^{33}-S(O)_2-NR^{32}R^{31}$ radical;

wherein each R^{30} is independently

(1) alkyl, alkenyl or alkynyl radicals optionally substituted by 1-3 radicals of $-CO_2R^{34}$, amino, alkylamino, dialkylamino, alkanoylamino, alkoxycarbonylamino, N-(alkoxycarbonyl)-N-(alkyl)amino, aminocarbonylamino, alkylsulfonylamino, hydroxy, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, cyano, halo or aralkoxy, arylalkylthio, arylalkylsulfonyl, cycloalkyl, heterocyclyl, aryl or heteroaryl radicals, wherein the cycloalkyl, heterocyclyl, aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of amino, alkylamino, dialkylamino, alkanoylamino, alkoxycarbonylamino, alkylsulfonylamino, alkanoyl, alkoxycarbonyl, hydroxy, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, cyano, halo, alkyl, haloalkyl or haloalkoxy;

(2) cycloalkyl or heterocyclyl radical optionally substituted by 1-3 radicals of amino, alkylamino, dialkylamino, alkanoylamino, alkoxycarbonylamino, alkylsulfonylamino, alkoxycarbonyl, hydroxy, alkoxy, alkylthio, cyano, alkyl, haloalkyl or haloalkoxy; or

(3) aryl or heteroaryl radicals optionally substituted by 1-3 radicals of amino, alkylamino, dialkylamino, alkanoylamino, alkoxycarbonylamino, alkylsulfonylamino, alkoxycarbonyl, hydroxy, alkoxy, alkylthio, cyano, halo, azido, alkyl, haloalkyl or haloalkoxy;

each R^{31} is independently hydrogen radical or R^{30};

wherein each R^{32} is independently

(1) hydrogen radicals;
(2) alkyl, alkenyl or alkynyl radicals optionally substituted by 1-3 radicals of amino, alkylamino, dialkylamino, hydroxy, alkoxy, alkylthio, cyano or halo; or
(3) aryl, heteroaryl, arylalkyl, heteroarylalkyl, heterocyclyl, heterocyclylalkyl, cycloalkyl or cycloalkylalkyl radicals optionally substituted by 1-3 radicals of amino, alkylamino, dialkylamino, hydroxy, alkoxy, alkylthio, cyano, alkyl, haloalkyl or haloalkoxy; and

each R^{33} is independently
(1) hydrogen radical;
(2) alkyl radical optionally substituted by a radical of heterocyclyl, aryl or heteroaryl which is optionally substituted by 1-3 radicals of amino, alkylamino, dialkylamino, alkanoylamino, alkoxycarbonylamino, alkylsulfonylamino, hydroxy, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, cyano, halo, alkyl, haloalkyl or haloalkoxy; or
(3) heterocyclyl, aryl or heteroaryl radicals optionally substituted by 1-3 radicals of amino, alkylamino, dialkylamino, alkanoylamino, alkoxycarbonylamino, alkylsulfonylamino, hydroxy, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, cyano, halo, alkyl, haloalkyl or haloalkoxy; and

each R^{34} is independently hydrogen, alkyl, aryl, heteroaryl, arylalkyl or heteroarylalkyl radicals, wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of amino, alkylamino, dialkylamino, alkanoylamino, alkoxycarbonylamino, alkylsulfonylamino, hydroxy, alkoxy, alkylthio, alkylsulfinyl, alkylsulfonyl, cyano, halo, alkyl, haloalkyl or haloalkoxy.

2. The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_1-C_{12} alkyl, C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, cycloalkyl or heterocyclyl radical optionally substituted by 1-3 radicals of -OH, -OR^3, -SR^3, -$S(O)R^3$, -$S(O)_2R^3$, -$C(O)R^3$, -NR^3R^4, aryl, heteroaryl, cycloalkyl or heterocyclyl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl, cycloalkyl and heterocyclyl radicals are optionally substituted by 1-3 radicals of hydroxy, -OR^3, -SR^3, -$S(O)R^3$, -$S(O)_2R^3$, -$C(O)R^3$, -NR^3R^4, amino, C_1-C_8 alkanoylamino, C_1-C_8 alkylsulfonylamino, C_1-C_8 alkoxycarbonylamino, C_1-C_8 alkoxycarbonyl, cyano, halo, azido, C_1-C_8 alkyl or C_1-C_8 haloalkyl of 1-3 halo radicals; provided that the total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^1 is 0-3;

wherein each R^3 is independently an C_1-C_8 alkyl, C_1-C_8 haloalkyl of 1-3 halo radicals, aryl, heteroaryl, aryl-C_1-C_4-alkyl or heteroaryl-C_1-C_4-alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, C_1-C_8 alkanoylamino, C_1-C_8 alkylsulfonylamino, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_1-C_8 alkoxycarbonylamino, C_1-C_8 alkoxycarbonyl, cyano, halo, azido, C_1-C_8 alkyl, C_1-C_8 haloalkyl of 1-3 halo radicals or C_1-C_8 haloalkoxy of 1-3 halo radicals; and each R^4 is independently a hydrogen or C_1-C_8 alkyl radical;

R^2 is a hydrogen or C_1-C_4 alkyl radical;

V is $-CHR^{11}-$ or $-CHR^{11}-CHR^{12}-$; wherein R^{11} and R^{12} are each independently (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, amino, C_1-C_8 alkanoylamino, C_1-C_8 alkylsulfonylamino, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_1-C_8 alkoxycarbonylamino, C_1-C_8 alkoxycarbonyl, cyano, halo, azido, C_1-C_8 alkyl, C_1-C_8 haloalkyl of 1-3 halo radicals or C_1-C_8 haloalkoxy of 1-3 halo radicals;

wherein each R^{20} is independently a hydrogen, C_1-C_8 alkyl, C_2-C_8 alkenyl, cycloalkyl, aryl, heteroaryl, aryl-C_1-C_4-alkyl, heteroaryl-C_1-C_4-alkyl, C_1-C_8 alkanoyl, aroyl or heteroaroyl radical; wherein the alkyl and alkenyl radicals are optionally substituted by $-C(O)R^{22}$; and wherein the cycloalkyl, aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, C_1-C_8 alkanoylamino, C_1-C_8 alkylsulfonylamino, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_1-C_8 alkoxycarbonylamino, C_1-C_8 alkoxycarbonyl, cyano, halo,

azido, C_1-C_8 alkyl, C_1-C_8 haloalkyl of 1-3 halo radicals or C_1-C_8 haloalkoxy of 1-3 halo radicals; and

each R^{21} is independently an C_1-C_8 alkyl, C_1-C_8 alkyl-C(O)R^{22}, aryl, heteroaryl, aryl-C_1-C_4-alkyl or heteroaryl-C_1-C_4-alkyl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, C_1-C_8 alkanoylamino, C_1-C_8 alkylsulfonylamino, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_1-C_8 alkoxycarbonylamino, C_1-C_8 alkoxycarbonyl, cyano, halo, azido, C_1-C_8 alkyl, C_1-C_8 haloalkyl of 1-3 halo radicals or C_1-C_8 haloalkoxy of 1-3 halo radicals;

wherein each R^{22} is independently a hydroxy, C_1-C_8 alkoxy, aryloxy, aryl-C_1-C_4-alkoxy, heteroaryloxy, heteroaryl-C_1-C_4-alkoxy or -$NR^{23}R^{24}$ radical; wherein R^{23} is a hydrogen, C_1-C_8 alkyl, aryl, aryl-C_1-C_4-alkyl, heteroaryl or heteroaryl-C_1-C_4-alkyl radical; and R^{24} is a hydrogen or C_1-C_8 alkyl radical; or -$NR^{23}R^{24}$ represents a heterocyclyl or heteroaryl radical; wherein the heterocyclyl, aryl and heteroaryl radicals of R^{22}, R^{23} and -$NR^{23}R^{24}$ are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, C_1-C_8 alkanoylamino, C_1-C_8 alkylsulfonylamino, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_1-C_8 alkoxycarbonylamino, C_1-C_8 alkoxycarbonyl, cyano, halo, azido, C_1-C_8 alkyl, C_1-C_8 haloalkyl of 1-3 halo radicals or C_1-C_8 haloalkoxy of 1-3 halo radicals; and

W-N represents -C(O)-N, -C(O)-$CR^{15}R^{16}$-N, -$CR^{15}R^{16}$-N or -$CR^{17}R^{18}$-$CR^{15}R^{16}$-N; wherein R^{15} and R^{16} are each

independently (1) a hydrogen, $-C(O)R^{22}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, C_1-C_8 alkanoylamino, C_1-C_8 alkylsulfonylamino, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_1-C_8 alkoxycarbonylamino, C_1-C_8 alkoxycarbonyl, cyano, halo, azido, C_1-C_8 alkyl, C_1-C_8 haloalkyl of 1-3 halo radicals or C_1-C_8 haloalkoxy of 1-3 halo radicals; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-3; and

R^{17} and R^{18} are each independently (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, C_1-C_8 alkanoylamino, C_1-C_8 alkylsulfonylamino, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_1-C_8 alkoxycarbonylamino, C_1-C_8 alkoxycarbonyl, cyano, halo, azido, C_1-C_8 alkyl, C_1-C_8 haloalkyl of 1-3 halo radicals or C_1-C_8 haloalkoxy of 1-3 halo radicals; or one of $-CR^{15}R^{16}-$ or $-CR^{17}R^{18}-$ represent a cycloalkylene or heterocyclylene radical; and

wherein each B is independently a

(1) bond;

(2) C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted by (a) 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, halo, and/or (b) 1-2 radicals of heterocyclyl, aryl or heteroaryl optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals;

(3) heterocyclyl radical optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals; or

(4) aryl or heteroaryl radical optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, halo, C_1-C_4 alkyl, C_1-C_8 haloalkyl of 1-3 halo radicals or C_1-C_8 haloalkoxy of 1-3 halo radicals;

wherein each R^{30} is independently

(1) C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radicals optionally substituted by 1-3 radicals of $-CO_2R^{34}$, amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5

alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, N-((C_1-C_4 alkoxy)carbonyl)-N-(C_1-C_4 alkyl)amino, aminocarbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, cyano, halo or aryl-C_1-C_4-alkoxy, aryl-C_1-C_4-alkylthio, aryl-C_1-C_4-alkylsulfonyl, C_3-C_8 cycloalkyl, heterocyclyl, aryl or heteroaryl radicals, wherein the cycloalkyl, heterocyclyl, aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, C_1-C_5 alkanoyl, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, cyano, halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals;

(2) cycloalkyl or heterocyclyl radical optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals; or

(3) aryl or heteroaryl radicals optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, halo, azido, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals;

each R^{31} is independently hydrogen radical or R^{30};

wherein each R^{32} is independently

(1) hydrogen radicals;

(2) C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radicals optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4-alkyl)amino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano or halo; or

(3) aryl, heteroaryl, aryl-C_1-C_4-alkyl, heteroaryl-C_1-C_4-alkyl, heterocyclyl, heterocyclyl-C_1-C_4-alkyl, C_3-C_8 cycloalkyl or C_3-C_8-cycloalkyl-C_1-C_4-alkyl radicals optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4-alkyl)amino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals; and

each R^{33} is independently

(1) hydrogen radical;

(2) C_1-C_4 alkyl radical optionally substituted by a radical of heterocyclyl, aryl or heteroaryl which is optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, cyano, halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals; or

(3) heterocyclyl, aryl or heteroaryl radicals optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, cyano, halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals; and

each R^{34} is independently hydrogen or C_1-C_4 alkyl, aryl, heteroaryl, aryl-C_1-C_4-alkyl or heteroaryl-C_1-C_4-alkyl radicals, wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, cyano, halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals; and

wherein cycloalkyl is a monocyclic, bicyclic or tricyclic carbocyclic alkyl radical of 3-10 ring members, which is optionally partially unsaturated or benzo-fused; cycloalkylene is a cycloalkyl gem divalent radical; heterocyclyl is a radical of a monocyclic or bicyclic saturated heterocyclic ring system having 5-8 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally partially unsaturated or benzo-fused and optionally substituted by 1-2 oxo or thioxo radicals; heterocyclylene is a heterocyclyl gem divalent radical on a ring carbon atom; aryl is a phenyl, biphenyl or naphthyl radical; and heteroaryl is radical of a monocyclic or bicyclic aromatic heterocyclic ring system having 5-6 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally benzo-fused or saturated C_3-C_4-carbocyclic-fused.

3. The compound of Claim 2 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_1-C_{12} alkyl, C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, cycloalkyl or heterocyclyl radical optionally substituted by 1-3 radicals of -OH, -OR^3, -SR^3, -$S(O)R^3$, -$S(O)_2R^3$, -$C(O)R^3$, -NR^3R^4, aryl, heteroaryl, cycloalkyl or heterocyclyl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl, cycloalkyl and heterocyclyl radicals are optionally substituted by 1-3 radicals of hydroxy, -OR^3, -SR^3, -$S(O)R^3$, -$S(O)_2R^3$, -$C(O)R^3$, -NR^3R^4, amino, C_1-C_4 alkanoylamino, C_1-C_4 alkylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_6 alkyl or C_1-C_4 haloalkyl of 1-3 halo radicals; provided that the total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^1 is 0-3;

wherein each R^3 is independently an C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals, aryl, heteroaryl, aryl-C_1-C_4-alkyl or heteroaryl-C_1-C_4-alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, C_1-C_4 alkanoylamino, C_1-C_4 alkylsulfonylamino, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals; and each R^4 is independently a hydrogen or C_1-C_4 alkyl radical;

V is -CHR^{11}- or -CHR^{11}-CHR^{12}-; wherein R^{11} and R^{12} are each independently (1) a hydrogen, -OR^{20}, -SR^{21}, -$C(O)R^{22}$, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-$S(O)_2$-R^{30}, -NR^{33}-$S(O)_2$-$NR^{32}R^{31}$, aryl or

heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, amino, C_1-C_4 alkanoylamino, C_1-C_4 alkylsulfonylamino, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals;

wherein each R^{20} is independently a hydrogen, C_1-C_4 alkyl, C_2-C_4 alkenyl, cycloalkyl, aryl, heteroaryl, aryl-C_1-C_4-alkyl, heteroaryl-C_1-C_4-alkyl, C_1-C_4 alkanoyl, aroyl or heteroaroyl radical; wherein the alkyl and alkenyl radicals are optionally substituted by $-C(O)R^{22}$; and wherein the cycloalkyl, aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, C_1-C_4 alkanoylamino, C_1-C_4 alkylsulfonylamino, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals; and

each R^{21} is independently an C_1-C_4 alkyl, C_1-C_4 alkyl-$C(O)R^{22}$, aryl, heteroaryl, aryl-C_1-C_4-alkyl or heteroaryl-C_1-C_4-alkyl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol,

amino, C_1-C_4 alkanoylamino, C_1-C_4 alkylsulfonylamino, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals;

wherein each R^{22} is independently a hydroxy, C_1-C_4 alkoxy, aryloxy, aryl-C_1-C_2-alkoxy, heteroaryloxy, heteroaryl-C_1-C_2-alkoxy or -$NR^{23}R^{24}$ radical; wherein R^{23} is a hydrogen, C_1-C_4 alkyl, aryl, aryl-C_1-C_2-alkyl, heteroaryl or heteroaryl-C_1-C_2-alkyl radical; and R^{24} is a hydrogen or C_1-C_4 alkyl radical; or -$NR^{23}R^{24}$ represents a heterocyclyl or heteroaryl radical; wherein the heterocyclyl, aryl and heteroaryl radicals of R^{22}, R^{23} and -$NR^{23}R^{24}$ are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, C_1-C_4 alkanoylamino, C_1-C_4 alkylsulfonylamino, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals; and

W-N represents -C(O)-N, -C(O)-$CR^{15}R^{16}$-N, -$CR^{15}R^{16}$-N or -$CR^{17}R^{18}$-$CR^{15}R^{16}$-N; wherein R^{15} and R^{16} are each independently (1) a hydrogen, -C(O)R^{22}, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted with an -OR^{20}, -SR^{21}, -C(O)R^{22}, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, C_1-C_4 alkanoylamino, C_1-C_4 alkylsulfonylamino, C_1-C_4 alkylsulfinyl, C_1-C_4

alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-3; and

R^{17} and R^{18} are each independently (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, C_1-C_4 alkanoylamino, C_1-C_4 alkylsulfonylamino, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals; or one of $-CR^{15}R^{16}-$ or $-CR^{17}R^{18}-$ represent a cycloalkylene or heterocyclylene radical; and

wherein each B is independently a
(1) bond;
(2) C_1-C_8 alkyl radical optionally substituted by (a) a radical of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio or cyano and/or (b) 1-3 halo radicals, and/or (c) 1-2 radicals of heterocyclyl, aryl or heteroaryl optionally substituted by 1-3

radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals;

(3) heterocyclyl radical; or

(4) aryl or heteroaryl radical optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, halo, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals;

wherein each R^{30} is independently

(1) C_1-C_6 alkyl radical optionally substituted by 1-3 radicals of $-CO_2R^{34}$, amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, N-((C_1-C_4 alkoxy)carbonyl)-N-(C_1-C_4 alkyl)amino, aminocarbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, cyano, halo or aryl-C_1-C_4-alkoxy, aryl-C_1-C_4-alkylthio, aryl-C_1-C_4-alkylsulfonyl, C_3-C_8 cycloalkyl, heterocyclyl, aryl or heteroaryl radicals, wherein the cycloalkyl, heterocyclyl, aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, C_1-C_5 alkanoyl, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, cyano, halo,

C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals;
(2) cycloalkyl or heterocyclyl radical optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals; or
(3) aryl or heteroaryl radicals optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, halo, azido, C_1-C_4 alkyl, C_1-C_4 haloalkyl of 1-3 halo radicals or C_1-C_4 haloalkoxy of 1-3 halo radicals;

each R^{31} is independently hydrogen radical or R^{30};

wherein each R^{32} is independently a hydrogen or C_1-C_4 alkyl radical; and

each R^{33} is independently a hydrogen or C_1-C_4 alkyl radical; and

each R^{34} is independently a hydrogen or C_1-C_4 alkyl radical; and

wherein cycloalkyl is a monocyclic, bicyclic or tricyclic carbocyclic alkyl radical of 3-10 ring members, which is optionally partially unsaturated or benzo-fused; cycloalkylene is a monocyclic cycloalkyl gem divalent radical of 3-6 ring members; heterocyclyl is a radical of a monocyclic or bicyclic saturated

heterocyclic ring system having 5-8 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally partially unsaturated or benzo-fused and optionally substituted by 1-2 oxo or thioxo radicals; heterocyclylene is a monocyclic heterocyclyl gem divalent radical on a ring carbon atom and having 5-6 ring members; aryl is a phenyl, biphenyl or naphthyl radical; and heteroaryl is radical of a monocyclic or bicyclic aromatic heterocyclic ring system having 5-6 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally benzo-fused or saturated C_3-C_4-carbocyclic-fused.

4. The compound of Claim 3 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_1-C_{12} alkyl or cycloalkyl radical optionally substituted by 1-3 radicals of -OH, $-OR^3$, $-SR^3$, $-S(O)R^3$, $-S(O)_2R^3$, $-C(O)R^3$, $-NR^3R^4$, aryl, heteroaryl, cycloalkyl or heterocyclyl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl, cycloalkyl and heterocyclyl radicals are optionally substituted by 1-3 radicals of hydroxy, $-OR^3$, $-SR^3$, $-S(O)R^3$, $-S(O)_2R^3$, $-C(O)R^3$, $-NR^3R^4$, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_6 alkyl or $-CF_3$ radicals; provided that the total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^1 is 0-3;

wherein each R^3 is independently an C_1-C_4 alkyl, $-CF_3$, aryl, heteroaryl, aryl-C_1-C_4-alkyl or heteroaryl-C_1-C_4-alkyl radical, wherein the aryl and heteroaryl radicals

are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$; and each R^4 is independently a hydrogen or methyl radical;

R^2 is a hydrogen radical;

V is $-CHR^{11}-$ or $-CHR^{11}-CHR^{12}-$; wherein R^{11} and R^{12} are each independently (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

wherein each R^{20} is independently a hydrogen, C_1-C_4 alkyl, C_2-C_4 alkenyl, cycloalkyl, aryl, heteroaryl, aryl-C_1-C_4-alkyl, heteroaryl-C_1-C_4-alkyl, C_1-C_4 alkanoyl, aroyl or heteroaroyl radical; wherein the alkyl and alkenyl radicals are optionally substituted by $-C(O)R^{22}$; and wherein the cycloalkyl, aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy,

C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

each R^{21} is independently an C_1-C_4 alkyl, C_1-C_4 alkyl-$C(O)R^{22}$, aryl, heteroaryl, aryl-C_1-C_4-alkyl or heteroaryl-C_1-C_4-alkyl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

wherein each R^{22} is independently a hydroxy, C_1-C_4 alkoxy, aryloxy, aryl-C_1-C_2-alkoxy, heteroaryloxy, heteroaryl-C_1-C_2-alkoxy or $-NR^{23}R^{24}$ radical; wherein R^{23} is a hydrogen, C_1-C_4 alkyl, aryl, aryl-C_1-C_2-alkyl, heteroaryl or heteroaryl-C_1-C_2-alkyl radical; and R^{24} is a hydrogen or C_1-C_4 alkyl radical; or $-NR^{23}R^{24}$ represents a heterocyclyl or heteroaryl radical; wherein the heterocyclyl, aryl and heteroaryl radicals of R^{22}, R^{23} and $-NR^{23}R^{24}$ are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

W-N represents -C(O)-N, $-C(O)-CR^{15}R^{16}-N$, $-CR^{15}R^{16}-N$ or $-CR^{17}R^{18}-CR^{15}R^{16}-N$; wherein R^{15} is (1) a hydrogen, $-C(O)R^{22}$,

aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted with an -OR^{20}, -SR^{21}, -$C(O)R^{22}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-3; and

R^{16} and R^{18} are each a hydrogen radical;

R^{17} is (1) a hydrogen, -OR^{20}, -SR^{21}, -$C(O)R^{22}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-$S(O)_2$-R^{30}, -NR^{33}-$S(O)_2$-$NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted with an -OR^{20}, -SR^{21}, -$C(O)R^{22}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-$S(O)_2$-R^{30}, -NR^{33}-$S(O)_2$-$NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals; or one of -$CR^{15}R^{16}$- or -$CR^{17}R^{18}$- represent a cycloalkylene or heterocyclylene radical; and

Z is O or S, X is CR^8 and Y is CR^9;

wherein R^8 and R^9 are each independently -B-A, provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^8 and R^9 is 0-3;

wherein each B is independently a
(1) bond;
(2) C_1-C_8 alkyl radical optionally substituted by (a) a radical of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, and/or (b) 1-3 halo radicals, and/or (c) 1-2 radicals of heterocyclyl, aryl or heteroaryl optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;
(3) heterocyclyl radical; or
(4) aryl or heteroaryl radical optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

each A is independently a
(1) hydrogen radical;
(2) halo, cyano or nitro radical;
(3) $-C(O)-R^{30}$, $-C(O)-OR^{31}$, $-C(O)-NR^{32}R^{31}$ or $-C(NR^{32})-NR^{32}R^{31}$ radical;
(4) $-OR^{31}$, $-O-C(O)-R^{31}$ or $-O-C(O)-NR^{32}R^{31}$ radical;

(5) $-SR^{31}$, $-S(O)-R^{30}$, $-S(O)_2-R^{30}$ or $-S(O)_2-NR^{32}R^{31}$ radical; or

(6) $-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(NR^{32})-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$ or $-NR^{33}-S(O)_2-NR^{32}R^{31}$ radical;

wherein each R^{30} is independently

(1) C_1-C_6 alkyl radical optionally substituted by 1-3 radicals of $-CO_2R^{34}$, amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, N-((C_1-C_4 alkoxy)carbonyl)-N-(C_1-C_4 alkyl)amino, aminocarbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, cyano, halo or aryl-C_1-C_4-alkoxy, aryl-C_1-C_4-alkylthio, aryl-C_1-C_4-alkylsulfonyl, C_3-C_8 cycloalkyl, heterocyclyl, aryl or heteroaryl radicals, wherein the cycloalkyl, heterocyclyl, aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, C_1-C_5 alkanoyl, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, cyano, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

(2) cycloalkyl or heterocyclyl radical optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, C_1-C_4 alkyl, C_1-C_2 haloalkyl of 1-3 halo radicals or $-OCF_3$; or

(3) aryl or heteroaryl radicals optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

each R^{31} is independently hydrogen radical or R^{30}; and

each R^{33} is independently a hydrogen or methyl radical.

5. The compound of Claim 4 or a pharmaceutically acceptable salt thereof, wherein

V is $-CHR^{11}-$; wherein R^{11} is (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals.

6. The compound of Claim 5 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_1-C_{12} alkyl or cycloalkyl radical optionally substituted by 1-3 radicals of -OH, -OR^3, -SR^3, -$S(O)_2R^3$, -NR^3R^4, aryl, heteroaryl, cycloalkyl or heterocyclyl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl, cycloalkyl and heterocyclyl radicals are optionally substituted by 1-3 radicals of hydroxy, -OR^3, -SR^3, -$S(O)_2R^3$, -NR^3R^4, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_6 alkyl or -CF_3 radicals; provided that the total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^1 is 0-2;

wherein each R^3 is independently an C_1-C_4 alkyl, -CF_3, aryl, heteroaryl, aryl-C_1-C_2-alkyl or heteroaryl-C_1-C_2-alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3;

V is -CHR^{11}-; wherein R^{11} is (1) a hydrogen, -OR^{20}, -SR^{21}, -C(O)R^{22}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-$S(O)_2$-R^{30}, -NR^{33}-$S(O)_2$-$NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an -OR^{20}, -SR^{21}, -C(O)R^{22}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-$S(O)_2$-R^{30}, -NR^{33}-$S(O)_2$-$NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2

radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, methylsulfonyl, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

wherein each R^{22} is independently a hydroxy, C_1-C_4 alkoxy, aryloxy, aryl-C_1-C_2-alkoxy, heteroaryloxy, heteroaryl-C_1-C_2-alkoxy or $-NR^{23}R^{24}$ radical; wherein R^{23} is a hydrogen, C_1-C_4 alkyl, aryl, aryl-C_1-C_2-alkyl, heteroaryl or heteroaryl-C_1-C_2-alkyl radical; and R^{24} is a hydrogen or C_1-C_4 alkyl radical; or $-NR^{23}R^{24}$ represents a heterocyclyl or heteroaryl radical; wherein the heterocyclyl, aryl and heteroaryl radicals of R^{22}, R^{23} and $-NR^{23}R^{24}$ are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

W-N represents $-C(O)-CR^{15}R^{16}-N$, $-CR^{15}R^{16}-N$ or $-CR^{17}R^{18}-CR^{15}R^{16}-N$; wherein R^{15} is (1) a hydrogen, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl radical optionally substituted with an $-OR^{20}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, C_1-C_4 alkoxycarbonylamino, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-2; and

R^{17} is (1) a hydrogen, $-OR^{20}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl, radical optionally substituted with an $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; wherein the

aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; or one of $-CR^{15}R^{16}-$ or $-CR^{17}R^{18}-$ represent a cycloalkylene or heterocyclylene radical; and

wherein R^8 is a radical of hydrogen, halo, C_1-C_2 alkoxy, amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, amidino, amido, carboxy, or C_1-C_4 alkyl optionally substituted by amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, 1-3 halo radicals, amidino, amido or carboxy radical; and

R^9 is -B-A, provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^9 is 0-2;

wherein each B is independently a
(1) bond;
(2) C_1-C_4 alkyl radical optionally substituted by (a) a radical of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, hydroxy or C_1-C_2 alkoxy, and/or (b) 1-2 halo radicals, and/or (c) a radical of heterocyclyl, aryl or heteroaryl optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_2 alkylsulfonylamino, hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthio, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;
(3) heterocyclyl radical; or

(4) aryl or heteroaryl radical optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_2 alkylsulfonylamino, hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthio, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

each A is independently a
(1) hydrogen radical;
(2) halo radical;
(3) $-C(O)-R^{30}$, $-C(O)-OR^{31}$, $-C(O)-NR^{32}R^{31}$ or $-C(NR^{32})-NR^{32}R^{31}$ radical;
(4) $-OR^{31}$ radical;
(5) $-SR^{31}$, $-S(O)_2-R^{30}$ or $-S(O)_2-NR^{32}R^{31}$ radical; or
(6) $-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$ or $-NR^{33}-S(O)_2-NR^{32}R^{31}$ radical;

wherein each R^{30} is independently
(1) $-CF_3$ or C_1-C_4 alkyl radical optionally substituted by 1-2 radicals of $-CO_2R^{34}$, amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, N-((C_1-C_4 alkoxy)carbonyl)-N-(C_1-C_4 alkyl)amino, hydroxy, C_1-C_4 alkoxy or aryl-C_1-C_2-alkoxy, heterocyclyl, aryl or heteroaryl radicals, wherein the heterocyclyl, aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_5 alkanoyl, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;
(2) cycloalkyl or heterocyclyl radical optionally substituted by 1-2 radicals of (C_1-C_4 alkoxy)carbonyl, hydroxy or C_1-C_4 alkyl; or

(3) aryl or heteroaryl radicals optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

each R^{31} is independently hydrogen radical or R^{30}; and

wherein cycloalkyl is a monocyclic carbocyclic alkyl radical of 3-6 ring members, which is optionally partially unsaturated or benzo-fused; cycloalkylene is a monocyclic cycloalkyl gem divalent radical of 3-6 ring members; heterocyclyl is a radical of a monocyclic saturated heterocyclic ring system having 5-8 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally partially unsaturated or benzo-fused and optionally substituted by 1-2 oxo or thioxo radicals; heterocyclylene is a monocyclic heterocyclyl gem divalent radical on a ring carbon atom and having 5-6 ring members; aryl is a phenyl, biphenyl or naphthyl radical; and heteroaryl is radical of a monocyclic or bicyclic aromatic heterocyclic ring system having 5-6 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally benzo-fused or saturated C_3-C_4-carbocyclic-fused.

7. The compound of Claim 6 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_1-C_{12} alkyl or cycloalkyl radical optionally substituted by 1-3 1-2 radicals of -OH, $-OR^3$, $-NR^3R^4$, aryl, heteroaryl or cycloalkyl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl and

cycloalkyl radicals are optionally substituted by 1-2 radicals of hydroxy, $-OR^{3}$, $-SR^{3}$, $-S(O)_2R^{3}$, $-NR^{3}R^{4}$, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, halo, C_1-C_6 alkyl or $-CF_3$ radicals; provided that the total number of aryl, heteroaryl and cycloalkyl radicals in R^{1} is 0-2;

wherein each R^{3} is independently an C_1-C_4 alkyl, $-CF_3$, aryl, heteroaryl, aryl-C_1-C_2-alkyl or heteroaryl-C_1-C_2-alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, methylsulfonylamino, C_1-C_2 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, halo, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$;

V is $-CHR^{11}-$; wherein R^{11} is (1) a hydrogen, $-OR^{20}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, aryloxy, heteroaryloxy, C_1-C_2 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals;

wherein each R^{20} is independently a hydrogen, C_1-C_4 alkyl-$C(O)R^{22}$, C_2-C_4 alkenyl, cycloalkyl, aryl, heteroaryl, aryl-C_1-C_2-alkyl, heteroaryl-C_1-C_2-alkyl or

C_1-C_4 alkanoyl radical; wherein the cycloalkyl, aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

each R^{21} is independently an C_1-C_4 alkyl, C_1-C_4 alkyl-$C(O)R^{22}$, aryl, heteroaryl, aryl-C_1-C_2-alkyl or heteroaryl-C_1-C_2-alkyl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals;

wherein each R^{22} is independently a hydroxy or $-NR^{23}R^{24}$ radical; wherein R^{23} is a hydrogen, C_1-C_2 alkyl, aryl, aryl-C_1-C_2-alkyl, heteroaryl or heteroaryl-C_1-C_2-alkyl radical; and R^{24} is a hydrogen or C_1-C_2 alkyl radical; or $-NR^{23}R^{24}$ represents a heteroaryl radical; wherein the aryl and heteroaryl radicals of R^{22}, R^{23} and $-NR^{23}R^{24}$ are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

W-N represents $-C(O)-CR^{15}R^{16}-N$, $-CR^{15}R^{16}-N$ or $-CR^{17}R^{18}-CR^{15}R^{16}-N$; wherein R^{15} is (1) a hydrogen, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl radical optionally substituted with an $-OR^{20}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, C_1-C_4 alkoxycarbonylamino, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; provided that the combined total number of

aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-2; and

R^{16} and R^{18} are each a hydrogen radical;

R^{17} is (1) a hydrogen, $-OR^{20}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl radical optionally substituted with an $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

wherein R^8 is a radical of hydrogen, halo, C_1-C_2 alkoxy, $-CF_3$ or C_1-C_4 alkyl optionally substituted by hydroxy or C_1-C_2 alkoxy radical; and

wherein each B is independently a
(1) bond;
(2) C_1-C_4 alkyl radical; or
(3) aryl or heteroaryl radical optionally substituted by a radical of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_2 alkylsulfonylamino, hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthio, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

each A is independently a
(1) hydrogen radical;
(2) halo radical;
(3) $-C(O)-R^{30}$, $-C(O)-OR^{31}$, $-C(O)-NR^{32}R^{31}$ or $-C(NR^{32})-NR^{32}R^{31}$ radical;

(4) $-OR^{31}$ radical;

(5) $-SR^{31}$, $-S(O)_2-R^{30}$ or $-S(O)_2-NR^{32}R^{31}$ radical; or

(6) $-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$ or $-NR^{33}-S(O)_2-R^{30}$ radical;

wherein each R^{30} is independently

(1) heterocyclyl radical optionally substituted by 1-2 radicals of (C_1-C_4 alkoxy)carbonyl, hydroxy or C_1-C_4 alkyl; or

(2) heteroaryl radicals optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

each R^{31} is independently

(1) hydrogen or $-CF_3$ radical;

(2) C_1-C_4 alkyl radical optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy or aryl-C_1-C_2-alkoxy, aryl or heteroaryl radicals, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_5 alkanoyl, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

(2) cycloalkyl radical optionally substituted by 1-2 radicals of hydroxy or C_1-C_4 alkyl; or

(3) aryl or heteroaryl radicals optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals.

8. The compound of Claim 7 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_1-C_{12} alkyl or cycloalkyl radical optionally substituted by 1-2 radicals of -OH, -OR^3, -NR^3R^4, aryl or heteroaryl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl and cycloalkyl radicals are optionally substituted by 1-2 radicals of hydroxy, -OR^3, -SR^3, -$S(O)_2R^3$, -NR^3R^4, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, halo, C_1-C_6 alkyl or -CF_3 radicals; provided that the total number of aryl, heteroaryl and cycloalkyl radicals in R^1 is 0-1;

wherein each R^3 is independently an C_1-C_4 alkyl, -CF_3, aryl, heteroaryl, arylmethyl or heteroarylmethyl radical;

V is -CHR^{11}-; wherein R^{11} is (1) a hydrogen, -OR^{20}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-$S(O)_2$-R^{30}, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an -OR^{20}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-$S(O)_2$-R^{30}, aryl or heteroaryl radical;

wherein each R^{20} is independently a hydrogen, C_2-C_4 alkenyl, cycloalkyl, aryl, heteroaryl, aryl-C_1-C_2-alkyl, heteroaryl-C_1-C_2-alkyl or C_1-C_4 alkanoyl radical; and

W-N represents -C(O)-$CR^{15}R^{16}$-N, -$CR^{15}R^{16}$-N or -$CR^{17}R^{18}$-$CR^{15}R^{16}$-N; wherein R^{15} is (1) a hydrogen, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl radical optionally substituted with an aryl or heteroaryl

radical; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-2; and

R^{17} is a hydrogen, hydroxy or C_1-C_4 alkyl radical; and

Z is S, X is CR^8 and Y is CR^9;

wherein R^8 is a radical of hydrogen, halo, C_1-C_2 alkoxy, $-CF_3$ or methyl; and

wherein each B is independently a
(1) bond;
(2) C_1-C_4 alkyl radical; or
(3) aryl or heteroaryl radical;

each A is independently a
(1) hydrogen radical;
(2) halo radical; or
(3) $-C(O)-R^{30}$, $-C(O)-OR^{31}$ or $-C(O)-NR^{32}R^{31}$ radical;

wherein each R^{30} is independently a heterocyclyl radical optionally substituted by C_1-C_4 alkyl;

each R^{31} is independently hydrogen radical or
(1) C_1-C_4 alkyl radical optionally substituted by 1-2 radicals of aryl or heteroaryl radicals, wherein the aryl and heteroaryl radicals are optionally substituted by a hydroxy, C_1-C_4 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radical; or
(2) cycloalkyl radical optionally substituted by 1-2 radicals of hydroxy or C_1-C_4 alkyl; or

(3) aryl or heteroaryl radicals optionally substituted by a hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radical.

9. The compound of Claim 8 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_5-C_{12} alkyl radical optionally substituted by 1-2 radicals of -OH, $-OR^3$ or $-NR^3R^4$; or (2) aryl or heteroaryl radicals optionally substituted by a hydroxy, $-OR^3$, $-SR^3$, $-S(O)_2R^3$, $-NR^3R^4$, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, halo, C_1-C_6 alkyl or $-CF_3$ radical; provided that the total number of aryl and heteroaryl radicals in R^1 is 0-1; and

wherein heterocyclyl is a radical of pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiamorpholinyl, 4-benzyl-piperazin-1-yl, pyrimidinyl, tetrahydrofuryl, pyrazolidonyl, pyrazolinyl, pyridazinonyl, pyrrolidonyl, tetrahydrothienyl or its sulfoxide or sulfone derivative, 2,3-dihydroindolyl, tetrahydroquinolinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydro-1-oxo-isoquinolinyl, 2,3-dihydrobenzofuryl, benzopyranyl, methylenedioxyphenyl or ethylenedioxyphenyl; aryl is a phenyl, biphenyl or naphthyl radical; and heteroaryl is radical of imidazolyl, pyrrolyl, pyrazolyl, pyridyl, pyrazinyl, triazolyl, furyl, thienyl, oxazolyl, thiazolyl, indolyl, quinolinyl, isoquinolinyl, 5,6,7,8-tetrahydroquinolyl, 5,6,7,8-tetrahydroisoquinolinyl, quinoxalinyl, benzothiazolyl, ß-carbolinyl, benzofuryl, benzimidazolyl or benzoxazolyl.

10. The compound of Claim 4 or a pharmaceutically acceptable salt thereof, wherein

V is $-CHR^{11}-CHR^{12}-$; wherein R^{11} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{12} is (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; or wherein R^{12} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{11} is (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl,

methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

W-N represents -C(O)-N or $-CR^{15}R^{16}$-N; wherein R^{15} is (1) a hydrogen, $-C(O)R^{22}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-3; and

R^{16} is a hydrogen radical; or $-CR^{15}R^{16}-$ represents a cycloalkylene or heterocyclylene radical.

11. The compound of Claim 10 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_1-C_{12} alkyl or cycloalkyl radical optionally substituted by 1-3 radicals of -OH, $-OR^3$, $-SR^3$, $-S(O)_2R^3$, $-NR^3R^4$, aryl, heteroaryl, cycloalkyl or heterocyclyl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl, cycloalkyl and heterocyclyl radicals are optionally substituted by 1-3 radicals of hydroxy, $-OR^3$, $-SR^3$, $-S(O)_2R^3$, $-NR^3R^4$, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo,

C_1-C_6 alkyl or -CF_3 radicals; provided that the total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^1 is 0-2;

wherein each R^3 is independently an C_1-C_4 alkyl, -CF_3, aryl, heteroaryl, aryl-C_1-C_2-alkyl or heteroaryl-C_1-C_2-alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3;

V is -CHR^{11}-CHR^{12}-; wherein R^{11} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{12} is (1) a hydrogen, -OR^{20}, -SR^{21}, -C(O)R^{22}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-S(O)$_2$-R^{30}, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an -OR^{20}, -SR^{21}, -C(O)R^{22}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-S(O)$_2$-R^{30}, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, methylsulfonyl, halo, azido, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals; or wherein R^{12} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{11} is (1) a hydrogen, -OR^{20}, -SR^{21}, -C(O)R^{22}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-S(O)$_2$-R^{30}, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl radical optionally substituted with

an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, methylsulfonyl, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

wherein each R^{22} is independently a hydroxy, C_1-C_4 alkoxy, aryloxy, aryl-C_1-C_2-alkoxy, heteroaryloxy, heteroaryl-C_1-C_2-alkoxy or $-NR^{23}R^{24}$ radical; wherein R^{23} is a hydrogen, C_1-C_4 alkyl, aryl, aryl-C_1-C_2-alkyl, heteroaryl or heteroaryl-C_1-C_2-alkyl radical; and R^{24} is a hydrogen or C_1-C_4 alkyl radical; or $-NR^{23}R^{24}$ represents a heterocyclyl or heteroaryl radical; wherein the heterocyclyl, aryl and heteroaryl radicals of R^{22}, R^{23} and $-NR^{23}R^{24}$ are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

W-N represents $-CR^{15}R^{16}-N$; wherein R^{15} is (1) a hydrogen, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl radical optionally substituted with an $-OR^{20}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, C_1-C_4 alkoxycarbonylamino, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; or $-CR^{15}R^{16}-$ represents a cycloalkylene or heterocyclylene radical; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-2; and

R^{16} is a hydrogen radical;

wherein R^8 is a radical of hydrogen, halo, C_1-C_2 alkoxy, amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, amidino, amido, carboxy, or C_1-C_4 alkyl optionally substituted by amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, 1-3 halo radicals, amidino, amido or carboxy radical; and

R^9 is -B-A, provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^9 is 0-2;

wherein each B is independently a
(1) bond;
(2) C_1-C_4 alkyl radical optionally substituted by (a) a radical of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, hydroxy or C_1-C_2 alkoxy, and/or (b) 1-2 halo radicals, and/or (c) a radical of heterocyclyl, aryl or heteroaryl optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_2 alkylsulfonylamino, hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthio, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;
(3) heterocyclyl radical; or
(4) aryl or heteroaryl radical optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_2 alkylsulfonylamino, hydroxy,

C_1-C_2 alkoxy, C_1-C_2 alkylthio, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

each A is independently a
(1) hydrogen radical;
(2) halo radical;
(3) $-C(O)-R^{30}$, $-C(O)-OR^{31}$, $-C(O)-NR^{32}R^{31}$ or $-C(NR^{32})-NR^{32}R^{31}$ radical;
(4) $-OR^{31}$ radical;
(5) $-SR^{31}$, $-S(O)_2-R^{30}$ or $-S(O)_2-NR^{32}R^{31}$ radical; or
(6) $-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$ or $-NR^{33}-S(O)_2-NR^{32}R^{31}$ radical;

wherein each R^{30} is independently
(1) $-CF_3$ or C_1-C_4 alkyl radical optionally substituted by 1-2 radicals of $-CO_2R^{34}$, amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, N-((C_1-C_4 alkoxy)carbonyl)-N-(C_1-C_4 alkyl)amino, hydroxy, C_1-C_4 alkoxy or aryl-C_1-C_2-alkoxy, heterocyclyl, aryl or heteroaryl radicals, wherein the heterocyclyl, aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_5 alkanoyl, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;
(2) cycloalkyl or heterocyclyl radical optionally substituted by 1-2 radicals of (C_1-C_4 alkoxy)carbonyl, hydroxy or C_1-C_4 alkyl; or
(3) aryl or heteroaryl radicals optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

each R^{31} is independently hydrogen radical or R^{30}; and

wherein cycloalkyl is a monocyclic carbocyclic alkyl radical of 3-6 ring members, which is optionally partially unsaturated or benzo-fused; cycloalkylene is a monocyclic cycloalkyl gem divalent radical of 3-6 ring members; heterocyclyl is a radical of a monocyclic saturated heterocyclic ring system having 5-8 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally partially unsaturated or benzo-fused and optionally substituted by 1-2 oxo or thioxo radicals; heterocyclylene is a monocyclic heterocyclyl gem divalent radical on a ring carbon atom and having 5-6 ring members; aryl is a phenyl, biphenyl or naphthyl radical; and heteroaryl is radical of a monocyclic or bicyclic aromatic heterocyclic ring system having 5-6 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally benzo-fused or saturated C_3-C_4-carbocyclic-fused.

12. The compound of Claim 11 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_1-C_{12} alkyl or cycloalkyl radical optionally substituted by 1-2 radicals of -OH, $-OR^3$, $-NR^3R^4$, aryl, heteroaryl or cycloalkyl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl and cycloalkyl radicals are optionally substituted by 1-2 radicals of hydroxy, $-OR^3$, $-SR^3$, $-S(O)_2R^3$, $-NR^3R^4$, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, halo, C_1-C_6

alkyl or $-CF_3$ radicals; provided that the total number of aryl, heteroaryl and cycloalkyl radicals in R^1 is 0-2;

wherein each R^3 is independently an C_1-C_4 alkyl, $-CF_3$, aryl, heteroaryl, aryl-C_1-C_2-alkyl or heteroaryl-C_1-C_2-alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, methylsulfonylamino, C_1-C_2 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, halo, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$;

V is $-CHR^{11}-CHR^{12}-$; wherein R^{11} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{12} is (1) a hydrogen, $-OR^{20}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, aryloxy, heteroaryloxy, C_1-C_2 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals; or wherein R^{12} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{11} is (1) a hydrogen, $-OR^{20}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, -O-

$C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, aryloxy, heteroaryloxy, C_1-C_2 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals;

wherein each R^{20} is independently a hydrogen, C_1-C_4 alkyl-$C(O)R^{22}$, C_2-C_4 alkenyl, cycloalkyl, aryl, heteroaryl, aryl-C_1-C_2-alkyl, heteroaryl-C_1-C_2-alkyl or C_1-C_4 alkanoyl radical; wherein the cycloalkyl, aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

each R^{21} is independently an C_1-C_4 alkyl, C_1-C_4 alkyl-$C(O)R^{22}$, aryl, heteroaryl, aryl-C_1-C_2-alkyl or heteroaryl-C_1-C_2-alkyl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals;

wherein each R^{22} is independently a hydroxy or $-NR^{23}R^{24}$ radical; wherein R^{23} is a hydrogen, C_1-C_2 alkyl, aryl, aryl-C_1-C_2-alkyl, heteroaryl or heteroaryl-C_1-C_2-alkyl radical; and R^{24} is a hydrogen or C_1-C_2 alkyl radical; or $-NR^{23}R^{24}$ represents a heteroaryl radical; wherein the aryl and heteroaryl radicals of R^{22}, R^{23} and $-NR^{23}R^{24}$ are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

W-N represents $-CR^{15}R^{16}-N$; wherein R^{15} is (1) a hydrogen, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl, radical optionally substituted with an $-OR^{20}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, C_1-C_4 alkoxycarbonylamino, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-2; and

R^{16} is a hydrogen radical;

wherein R^8 is a radical of hydrogen, halo, C_1-C_2 alkoxy, $-CF_3$ or C_1-C_4 alkyl optionally substituted by hydroxy or C_1-C_2 alkoxy radical; and

wherein each B is independently a
(1) bond;
(2) C_1-C_4 alkyl radical; or
(3) aryl or heteroaryl radical optionally substituted by a radical of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_2 alkylsulfonylamino, hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthio, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

each A is independently a
(1) hydrogen radical;
(2) halo radical;
(3) $-C(O)-R^{30}$, $-C(O)-OR^{31}$, $-C(O)-NR^{32}R^{31}$ or $-C(NR^{32})-NR^{32}R^{31}$ radical;
(4) $-OR^{31}$ radical;

(5) $-SR^{31}$, $-S(O)_2-R^{30}$ or $-S(O)_2-NR^{32}R^{31}$ radical; or

(6) $-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$ or $-NR^{33}-S(O)_2-R^{30}$ radical;

wherein each R^{30} is independently

(1) heterocyclyl radical optionally substituted by 1-2 radicals of (C_1-C_4 alkoxy)carbonyl, hydroxy or C_1-C_4 alkyl; or

(2) heteroaryl radicals optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

each R^{31} is independently

(1) hydrogen or $-CF_3$ radical;

(2) C_1-C_4 alkyl radical optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy or aryl-C_1-C_2-alkoxy, aryl or heteroaryl radicals, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_5 alkanoyl, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

(3) cycloalkyl radical optionally substituted by 1-2 radicals of hydroxy or C_1-C_4 alkyl; or

(4) aryl or heteroaryl radicals optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals.

13. The compound of Claim 12 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_5-C_{12} alkyl radical optionally substituted by 1-2 radicals of -OH, $-OR^3$ or $-NR^3R^4$; or (2) aryl or heteroaryl radical optionally substituted by a hydroxy, $-OR^3$, $-SR^3$, $-S(O)_2R^3$, $-NR^3R^4$, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, halo, C_1-C_6 alkyl or $-CF_3$ radicals; provided that the total number of aryl, heteroaryl and cycloalkyl radicals in R^1 is 0-1;

wherein each R^3 is independently an C_1-C_4 alkyl, $-CF_3$, aryl, heteroaryl, arylmethyl or heteroarylmethyl radical;

V is $-CHR^{11}-CHR^{12}-$; wherein R^{11} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{12} is (1) a hydrogen, $-OR^{20}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or wherein R^{12} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{11} is (1) a hydrogen, $-OR^{20}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical;

wherein each R^{20} is independently a hydrogen, C_2-C_4 alkenyl, cycloalkyl, aryl, heteroaryl, aryl-C_1-C_2-alkyl, heteroaryl-C_1-C_2-alkyl or C_1-C_4 alkanoyl radical; and

W-N represents -$CR^{15}R^{16}$-N; wherein R^{15} is (1) a hydrogen, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl, radical optionally substituted with an aryl or heteroaryl radical; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-2; and

Z is S, X is CR^8 and Y is CR^9;

wherein R^8 is a radical of hydrogen, halo, C_1-C_2 alkoxy, -CF_3 or methyl; and

wherein each B is independently a
(1) bond;
(2) C_1-C_4 alkyl radical; or
(3) aryl or heteroaryl radical;

each A is independently a
(1) hydrogen radical;
(2) halo radical; or
(3) -C(O)-R^{30}, -C(O)-OR^{31} or -C(O)-$NR^{32}R^{31}$ radical;

wherein each R^{30} is independently heterocyclyl radical optionally substituted by C_1-C_4 alkyl;

each R^{31} is independently
(1) hydrogen radical;
(2) C_1-C_4 alkyl radical optionally substituted by 1-2 radicals of aryl or heteroaryl radicals, wherein the aryl and heteroaryl radicals are optionally substituted

by a hydroxy, C_1-C_4 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; or

(2) cycloalkyl radical optionally substituted by 1-2 radicals of hydroxy or C_1-C_4 alkyl; or

(3) aryl or heteroaryl radicals optionally substituted by a hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

wherein heterocyclyl is a radical of pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiamorpholinyl, 4-benzyl-piperazin-1-yl, pyrimidinyl, tetrahydrofuryl, pyrazolidonyl, pyrazolinyl, pyridazinonyl, pyrrolidonyl, tetrahydrothienyl or its sulfoxide or sulfone derivative, 2,3-dihydroindolyl, tetrahydroquinolinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydro-1-oxo-isoquinolinyl, 2,3-dihydrobenzofuryl, benzopyranyl, methylenedioxyphenyl or ethylenedioxyphenyl; aryl is a phenyl, biphenyl or naphthyl radical; and heteroaryl is radical of imidazolyl, pyrrolyl, pyrazolyl, pyridyl, pyrazinyl, triazolyl, furyl, thienyl, oxazolyl, thiazolyl, indolyl, quinolinyl, isoquinolinyl, 5,6,7,8-tetrahydroquinolyl, 5,6,7,8-tetrahydroisoquinolinyl, quinoxalinyl, benzothiazolyl, ß-carbolinyl, benzofuryl, benzimidazolyl or benzoxazolyl.

14. The compound of Claim 3 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_1-C_{12} alkyl or cycloalkyl radical optionally substituted by 1-3 radicals of -OH, $-OR^3$, $-SR^3$, $-S(O)R^3$, $-S(O)_2R^3$, $-C(O)R^3$, $-NR^3R^4$, aryl, heteroaryl, cycloalkyl or heterocyclyl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl, cycloalkyl and heterocyclyl radicals are optionally substituted by 1-3

radicals of hydroxy, $-OR^3$, $-SR^3$, $-S(O)R^3$, $-S(O)_2R^3$, $-C(O)R^3$, $-NR^3R^4$, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_6 alkyl or $-CF_3$ radicals; provided that the total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^1 is 0-3;

wherein each R^3 is independently an C_1-C_4 alkyl, $-CF_3$, aryl, heteroaryl, aryl-C_1-C_4-alkyl or heteroaryl-C_1-C_4-alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$; and each R^4 is independently a hydrogen or methyl radical;

R^2 is a hydrogen radical;

V is $-CHR^{11}-$ or $-CHR^{11}-CHR^{12}-$; wherein R^{11} and R^{12} are each independently (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-

C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

wherein each R^{20} is independently a hydrogen, C_1-C_4 alkyl, C_2-C_4 alkenyl, cycloalkyl, aryl, heteroaryl, aryl-C_1-C_4-alkyl, heteroaryl-C_1-C_4-alkyl, C_1-C_4 alkanoyl, aroyl or heteroaroyl radical; wherein the alkyl and alkenyl radicals are optionally substituted by $-C(O)R^{22}$; and wherein the cycloalkyl, aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

each R^{21} is independently an C_1-C_4 alkyl, C_1-C_4 alkyl-$C(O)R^{22}$, aryl, heteroaryl, aryl-C_1-C_4-alkyl or heteroaryl-C_1-C_4-alkyl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

wherein each R^{22} is independently a hydroxy, C_1-C_4 alkoxy, aryloxy, aryl-C_1-C_2-alkoxy, heteroaryloxy, heteroaryl-C_1-C_2-alkoxy or $-NR^{23}R^{24}$ radical; wherein R^{23} is a hydrogen, C_1-C_4 alkyl, aryl, aryl-C_1-C_2-alkyl, heteroaryl or heteroaryl-C_1-C_2-alkyl radical; and R^{24} is a hydrogen or C_1-C_4 alkyl radical; or $-NR^{23}R^{24}$ represents a heterocyclyl or heteroaryl radical; wherein the heterocyclyl, aryl and heteroaryl radicals of R^{22}, R^{23}

and $-NR^{23}R^{24}$ are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

W-N represents -C(O)-N, $-C(O)-CR^{15}R^{16}-N$, $-CR^{15}R^{16}-N$ or $-CR^{17}R^{18}-CR^{15}R^{16}-N$; wherein R^{15} is (1) a hydrogen, $-C(O)R^{22}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-3; and

R^{16} and R^{18} are each a hydrogen radical;

R^{17} is (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally

substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; or one of $-CR^{15}R^{16}-$ or $-CR^{17}R^{18}-$ represent a cycloalkylene or heterocyclylene radical; and

X is O or S, Y is CR^9 and Z is CR^{10};

wherein R^9 and R^{10} are each independently -B-A, provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^9 and R^{10} is 0-3;

wherein each B is independently a
(1) bond;
(2) C_1-C_8 alkyl radical optionally substituted by (a) a radical of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio or cyano, and/or (b) 1-3 halo radicals, and/or (c) 1-2 radicals of heterocyclyl, aryl or heteroaryl optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;
(3) heterocyclyl radical; or
(4) aryl or heteroaryl radical optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy,

C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

each A is independently a
(1) hydrogen radical;
(2) halo, cyano or nitro radical;
(3) $-C(O)-R^{30}$, $-C(O)-OR^{31}$, $-C(O)-NR^{32}R^{31}$ or $-C(NR^{32})-NR^{32}R^{31}$ radical;
(4) $-OR^{31}$, $-O-C(O)-R^{31}$ or $-O-C(O)-NR^{32}R^{31}$ radical;
(5) $-SR^{31}$, $-S(O)-R^{30}$, $-S(O)_2-R^{30}$ or $-S(O)_2-NR^{32}R^{31}$ radical; or
(6) $-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(NR^{32})-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$ or $-NR^{33}-S(O)_2-NR^{32}R^{31}$ radical;

wherein each R^{30} is independently
(1) C_1-C_6 alkyl radical optionally substituted by 1-3 radicals of $-CO_2R^{34}$, amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, N-((C_1-C_4 alkoxy)carbonyl)-N-(C_1-C_4 alkyl)amino, aminocarbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, cyano, halo or aryl-C_1-C_4-alkoxy, aryl-C_1-C_4-alkylthio, aryl-C_1-C_4-alkylsulfonyl, C_3-C_8 cycloalkyl, heterocyclyl, aryl or heteroaryl radicals, wherein the cycloalkyl, heterocyclyl, aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, C_1-C_5 alkanoyl, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio,

C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, cyano, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;
(2) cycloalkyl or heterocyclyl radical optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, C_1-C_4 alkyl, C_1-C_2 haloalkyl of 1-3 halo radicals or $-OCF_3$; or
(3) aryl or heteroaryl radicals optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

each R^{31} is independently hydrogen radical or R^{30}; and

each R^{33} is independently a hydrogen or methyl radical.

15. The compound of Claim 14 or a pharmaceutically acceptable salt thereof, wherein

V is $-CHR^{11}-$; wherein R^{11} is (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2

radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

W-N represents -C(O)-N, -C(O)-$CR^{15}R^{16}$-N, -$CR^{15}R^{16}$-N or -$CR^{17}R^{18}$-$CR^{15}R^{16}$-N; wherein R^{15} is (1) a hydrogen, -C(O)R^{22}, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted with an -OR^{20}, -SR^{21}, -C(O)R^{22}, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-3; and

wherein R^9 is independently -B-A; and
wherein R^{10} is independently -B-A when R^{11} is a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical; and when R^{11} is other than a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical, then R^{10} is independently a radical of hydrogen, halo, C_1-C_2 alkoxy, amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, amidino, amido, carboxy, or C_1-C_4 alkyl optionally substituted by amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, 1-3 halo radicals, amidino, amido or carboxy radical; and provided that the combined total number of aryl,

heteroaryl, cycloalkyl and heterocyclyl radicals in R^9 and R^{10} is 0-3.

16. The compound of Claim 15 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_1-C_{12} alkyl or cycloalkyl radical optionally substituted by 1-3 radicals of -OH, $-OR^3$, $-SR^3$, $-S(O)_2R^3$, $-NR^3R^4$, aryl, heteroaryl, cycloalkyl or heterocyclyl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl, cycloalkyl and heterocyclyl radicals are optionally substituted by 1-3 radicals of hydroxy, $-OR^3$, $-SR^3$, $-S(O)_2R^3$, $-NR^3R^4$, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_6 alkyl or $-CF_3$ radicals; provided that the total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^1 is 0-2;

wherein each R^3 is independently an C_1-C_4 alkyl, $-CF_3$, aryl, heteroaryl, aryl-C_1-C_2-alkyl or heteroaryl-C_1-C_2-alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$;

V is $-CHR^{11}-$; wherein R^{11} is (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$,

aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, methylsulfonyl, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

wherein each R^{22} is independently a hydroxy, C_1-C_4 alkoxy, aryloxy, aryl-C_1-C_2-alkoxy, heteroaryloxy, heteroaryl-C_1-C_2-alkoxy or $-NR^{23}R^{24}$ radical; wherein R^{23} is a hydrogen, C_1-C_4 alkyl, aryl, aryl-C_1-C_2-alkyl, heteroaryl or heteroaryl-C_1-C_2-alkyl radical; and R^{24} is a hydrogen or C_1-C_4 alkyl radical; or $-NR^{23}R^{24}$ represents a heterocyclyl or heteroaryl radical; wherein the heterocyclyl, aryl and heteroaryl radicals of R^{22}, R^{23} and $-NR^{23}R^{24}$ are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

W-N represents $-C(O)-CR^{15}R^{16}-N$, $-CR^{15}R^{16}-N$ or $-CR^{17}R^{18}-CR^{15}R^{16}-N$; wherein R^{15} is (1) a hydrogen, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl radical optionally substituted with an $-OR^{20}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, C_1-C_4 alkoxycarbonylamino, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; provided that the combined total number of

aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-2; and

R^{17} is (1) a hydrogen, $-OR^{20}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl, radical optionally substituted with an $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; or one of $-CR^{15}R^{16}-$ or $-CR^{17}R^{18}-$ represent a cycloalkylene or heterocyclylene radical; and

wherein each B is independently a
(1) bond;
(2) C_1-C_4 alkyl radical optionally substituted by (a) a radical of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, hydroxy or C_1-C_2 alkoxy, and/or (b) 1-2 halo radicals, and/or (c) a radical of heterocyclyl, aryl or heteroaryl optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_2 alkylsulfonylamino, hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthio, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;
(3) heterocyclyl radical; or
(4) aryl or heteroaryl radical optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_2 alkylsulfonylamino, hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthio, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

each A is independently a
(1) hydrogen radical;
(2) halo radical;
(3) $-C(O)-R^{30}$, $-C(O)-OR^{31}$, $-C(O)-NR^{32}R^{31}$ or $-C(NR^{32})-NR^{32}R^{31}$ radical;
(4) $-OR^{31}$ radical;
(5) $-SR^{31}$, $-S(O)_2-R^{30}$ or $-S(O)_2-NR^{32}R^{31}$ radical; or
(6) $-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$ or $-NR^{33}-S(O)_2-NR^{32}R^{31}$ radical;

wherein each R^{30} is independently
(1) $-CF_3$ or C_1-C_4 alkyl radical optionally substituted by 1-2 radicals of $-CO_2R^{34}$, amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, N-((C_1-C_4 alkoxy)carbonyl)-N-(C_1-C_4 alkyl)amino, hydroxy, C_1-C_4 alkoxy, aryl-C_1-C_2-alkoxy, heterocyclyl, aryl or heteroaryl radicals, wherein the heterocyclyl, aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_5 alkanoyl, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;
(2) cycloalkyl or heterocyclyl radical optionally substituted by 1-2 radicals of (C_1-C_4 alkoxy)carbonyl, hydroxy or C_1-C_4 alkyl; or
(3) aryl or heteroaryl radicals optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

each R^{31} is independently hydrogen radical or R^{30}; and

wherein cycloalkyl is a monocyclic carbocyclic alkyl radical of 3-6 ring members, which is optionally partially unsaturated or benzo-fused; cycloalkylene is a monocyclic cycloalkyl gem divalent radical of 3-6 ring members; heterocyclyl is a radical of a monocyclic saturated heterocyclic ring system having 5-8 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally partially unsaturated or benzo-fused and optionally substituted by 1-2 oxo or thioxo radicals; heterocyclylene is a monocyclic heterocyclyl gem divalent radical on a ring carbon atom and having 5-6 ring members; aryl is a phenyl, biphenyl or naphthyl radical; and heteroaryl is radical of a monocyclic or bicyclic aromatic heterocyclic ring system having 5-6 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally benzo-fused or saturated C_3-C_4-carbocyclic-fused.

17. The compound of Claim 16 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_1-C_{12} alkyl or cycloalkyl radical optionally substituted by 1-2 radicals of -OH, -OR^3, -NR^3R^4, aryl, heteroaryl or cycloalkyl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl and cycloalkyl radicals are optionally substituted by 1-2 radicals of hydroxy, -OR^3, -SR^3, -$S(O)_2R^3$, -NR^3R^4, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, halo, C_1-C_6 alkyl or -CF_3 radicals; provided that the total number

of aryl, heteroaryl and cycloalkyl radicals in R^1 is 0-2;

wherein each R^3 is independently an C_1-C_4 alkyl, $-CF_3$, aryl, heteroaryl, aryl-C_1-C_2-alkyl or heteroaryl-C_1-C_2-alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, methylsulfonylamino, C_1-C_2 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, halo, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$;

V is $-CHR^{11}-$; wherein R^{11} is (1) a hydrogen, $-OR^{20}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, aryloxy, heteroaryloxy, C_1-C_2 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals;

wherein each R^{20} is independently a hydrogen, C_1-C_4 alkyl-$C(O)R^{22}$, C_2-C_4 alkenyl, cycloalkyl, aryl, heteroaryl, aryl-C_1-C_2-alkyl, heteroaryl-C_1-C_2-alkyl or C_1-C_4 alkanoyl radical; wherein the cycloalkyl, aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

each R^{21} is independently an C_1-C_4 alkyl, C_1-C_4 alkyl-C(O)R^{22}, aryl, heteroaryl, aryl-C_1-C_2-alkyl or heteroaryl-C_1-C_2-alkyl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, halo, azido, C_1-C_2 alkyl, -CF_3 or -OCF_3 radicals;

wherein each R^{22} is independently a hydroxy or -$NR^{23}R^{24}$ radical; wherein R^{23} is a hydrogen, C_1-C_2 alkyl, aryl, aryl-C_1-C_2-alkyl, heteroaryl or heteroaryl-C_1-C_2-alkyl radical; and R^{24} is a hydrogen or C_1-C_2 alkyl radical; or -$NR^{23}R^{24}$ represents a heteroaryl radical; wherein the aryl and heteroaryl radicals of R^{22}, R^{23} and -$NR^{23}R^{24}$ are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, halo, azido, C_1-C_2 alkyl, -CF_3 or -OCF_3 radicals; and

W-N represents -C(O)-$CR^{15}R^{16}$-N, -$CR^{15}R^{16}$-N or -$CR^{17}R^{18}$-$CR^{15}R^{16}$-N; wherein R^{15} is (1) a hydrogen, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl radical optionally substituted with an -OR^{20}, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, C_1-C_4 alkoxycarbonylamino, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-2; and

R^{16} and R^{18} are each a hydrogen radical;

R^{17} is (1) a hydrogen, $-OR^{20}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl radical optionally substituted with an $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

wherein R^9 is independently -B-A; and
wherein R^{10} is independently -B-A when R^{11} is a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical; and when R^{11} is other than a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical, then R^{10} is independently a radical of hydrogen, halo, C_1-C_2 alkoxy, $-CF_3$ or C_1-C_4 alkyl optionally substituted by hydroxy or C_1-C_2 alkoxy radical; and provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^9 and R^{10} is 0-3;

wherein each B is independently a
(1) bond;
(2) C_1-C_4 alkyl radical; or
(3) aryl or heteroaryl radical optionally substituted by a radical of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_2 alkylsulfonylamino, hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthio, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

each A is independently a
(1) hydrogen radical;

(2) halo radical;

(3) $-C(O)-R^{30}$, $-C(O)-OR^{31}$, $-C(O)-NR^{32}R^{31}$ or $-C(NR^{32})-NR^{32}R^{31}$ radical;

(4) $-OR^{31}$ radical;

(5) $-SR^{31}$, $-S(O)_2-R^{30}$ or $-S(O)_2-NR^{32}R^{31}$ radical; or

(6) $-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$ or $-NR^{33}-S(O)_2-R^{30}$ radical;

wherein each R^{30} is independently

(1) heterocyclyl radical optionally substituted by 1-2 radicals of (C_1-C_4 alkoxy)carbonyl, hydroxy or C_1-C_4 alkyl; or

(2) heteroaryl radicals optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

each R^{31} is independently

(1) hydrogen or $-CF_3$ radical;

(2) C_1-C_4 alkyl radical optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, aryl-C_1-C_2-alkoxy, aryl or heteroaryl radicals, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_5 alkanoyl, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

(3) cycloalkyl radical optionally substituted by 1-2 radicals of hydroxy or C_1-C_4 alkyl; or

(4) aryl or heteroaryl radicals optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals.

18. The compound of Claim 17 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_1-C_{12} alkyl or cycloalkyl radical optionally substituted by 1-2 radicals of -OH, $-OR^3$, $-NR^3R^4$, aryl or heteroaryl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl and cycloalkyl radicals are optionally substituted by 1-2 radicals of hydroxy, $-OR^3$, $-SR^3$, $-S(O)_2R^3$, $-NR^3R^4$, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, halo, C_1-C_6 alkyl or $-CF_3$ radicals; provided that the total number of aryl, heteroaryl and cycloalkyl radicals in R^1 is 0-1;

wherein each R^3 is independently an C_1-C_4 alkyl, $-CF_3$, aryl, heteroaryl, arylmethyl or heteroarylmethyl radical;

V is $-CHR^{11}-$; wherein R^{11} is (1) a hydrogen, $-OR^{20}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical;

wherein each R^{20} is independently a hydrogen, C_2-C_4 alkenyl, cycloalkyl, aryl, heteroaryl, aryl-C_1-C_2-alkyl, heteroaryl-C_1-C_2-alkyl or C_1-C_4 alkanoyl radical; and

W-N represents $-C(O)-CR^{15}R^{16}-N$, $-CR^{15}R^{16}-N$ or $-CR^{17}R^{18}-CR^{15}R^{16}-N$; wherein R^{15} is (1) a hydrogen, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl radical optionally substituted with an aryl or heteroaryl radical; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-2; and

R^{17} is a hydrogen, hydroxy or C_1-C_4 alkyl radical; and

X is S, Y is CR^9 and Z is CR^{10};

wherein R^9 is independently -B-A; and wherein R^{10} is independently -B-A when R^{11} is a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical; and when R^{11} is other than a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical, then R^{10} is independently a radical of hydrogen, halo, C_1-C_2 alkoxy, $-CF_3$ or methyl radical; and provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^9 and R^{10} is 0-3;

wherein each B is independently a
(1) bond;
(2) C_1-C_4 alkyl radical; or
(3) aryl or heteroaryl radical;

each A is independently a
(1) hydrogen radical;
(2) halo radical; or
(3) $-C(O)-R^{30}$, $-C(O)-OR^{31}$ or $-C(O)-NR^{32}R^{31}$ radical;

wherein each R^{30} is independently a heterocyclyl radical optionally substituted by C_1-C_4 alkyl; and

each R^{31} is independently hydrogen radical or (1) C_1-C_4 alkyl radical optionally substituted by 1-2 radicals of aryl or heteroaryl radicals, wherein the aryl and heteroaryl radicals are optionally substituted by a hydroxy, C_1-C_4 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radical; or (2) cycloalkyl radical optionally substituted by 1-2 radicals of hydroxy or C_1-C_4 alkyl; or (3) aryl or heteroaryl radicals optionally substituted by a hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radical.

19. The compound of Claim 18 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_5-C_{12} alkyl radical optionally substituted by 1-2 radicals of $-OH$, $-OR^3$ or $-NR^3R^4$; or (2) aryl or heteroaryl radicals optionally substituted by a hydroxy, $-OR^3$, $-SR^3$, $-S(O)_2R^3$, $-NR^3R^4$, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, halo, C_1-C_6 alkyl or $-CF_3$ radical; provided that the total number of aryl and heteroaryl radicals in R^1 is 0-1; and

wherein heterocyclyl is a radical of pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiamorpholinyl, 4-benzyl-piperazin-1-yl, pyrimidinyl, tetrahydrofuryl, pyrazolidonyl, pyrazolinyl, pyridazinonyl, pyrrolidonyl, tetrahydrothienyl or its sulfoxide or sulfone derivative, 2,3-dihydroindolyl, tetrahydroquinolinyl,

1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydro-1-oxo-isoquinolinyl, 2,3-dihydrobenzofuryl, benzopyranyl, methylenedioxyphenyl or ethylenedioxyphenyl; aryl is a phenyl, biphenyl or naphthyl radical; and heteroaryl is radical of imidazolyl, pyrrolyl, pyrazolyl, pyridyl, pyrazinyl, triazolyl, furyl, thienyl, oxazolyl, thiazolyl, indolyl, quinolinyl, isoquinolinyl, 5,6,7,8-tetrahydroquinolyl, 5,6,7,8-tetrahydroisoquinolinyl, quinoxalinyl, benzothiazolyl, ß-carbolinyl, benzofuryl, benzimidazolyl or benzoxazolyl.

20. The compound of Claim 14 or a pharmaceutically acceptable salt thereof, wherein

V is $-CHR^{11}-CHR^{12}-$; wherein R^{11} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{12} is (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; or wherein R^{12} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{11} is (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-$

$C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

W-N represents -C(O)-N or $-CR^{15}R^{16}-N$; wherein R^{15} is (1) a hydrogen, $-C(O)R^{22}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-3; and

R^{16} is a hydrogen radical; or $-CR^{15}R^{16}-$ represents a cycloalkylene or heterocyclylene radical; and

wherein R^9 is independently -B-A; and

wherein R^{10} is independently -B-A when R^{11} and R^{12} are each independently a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical; and when R^{11} or R^{12} is independently other than a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical, then R^{10} is independently a radical of hydrogen, halo, C_1-C_2 alkoxy, amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, amidino, amido, carboxy, or C_1-C_4 alkyl optionally substituted by amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, 1-3 halo radicals, amidino, amido or carboxy radical; and provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^9 and R^{10} is 0-3.

21. The compound of Claim 20 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_1-C_{12} alkyl or cycloalkyl radical optionally substituted by 1-3 radicals of -OH, -OR^3, -SR^3, -$S(O)_2R^3$, -NR^3R^4, aryl, heteroaryl, cycloalkyl or heterocyclyl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl, cycloalkyl and heterocyclyl radicals are optionally substituted by 1-3 radicals of hydroxy, -OR^3, -SR^3, -$S(O)_2R^3$, -NR^3R^4, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_6 alkyl or -CF_3 radicals; provided that the total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^1 is 0-2;

wherein each R^3 is independently an C_1-C_4 alkyl, -CF_3, aryl, heteroaryl, aryl-C_1-C_2-alkyl or heteroaryl-C_1-C_2-

alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$;

V is $-CHR^{11}-CHR^{12}-$; wherein R^{11} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{12} is (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, methylsulfonyl, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; or wherein R^{12} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{11} is (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4

alkylthiol, methylsulfonyl, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

wherein each R^{22} is independently a hydroxy, C_1-C_4 alkoxy, aryloxy, aryl-C_1-C_2-alkoxy, heteroaryloxy, heteroaryl-C_1-C_2-alkoxy or $-NR^{23}R^{24}$ radical; wherein R^{23} is a hydrogen, C_1-C_4 alkyl, aryl, aryl-C_1-C_2-alkyl, heteroaryl or heteroaryl-C_1-C_2-alkyl radical; and R^{24} is a hydrogen or C_1-C_4 alkyl radical; or $-NR^{23}R^{24}$ represents a heterocyclyl or heteroaryl radical; wherein the heterocyclyl, aryl and heteroaryl radicals of R^{22}, R^{23} and $-NR^{23}R^{24}$ are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

W-N represents $-CR^{15}R^{16}$-N; wherein R^{15} is (1) a hydrogen, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl radical optionally substituted with an $-OR^{20}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, C_1-C_4 alkoxycarbonylamino, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; or $-CR^{15}R^{16}$- represents a cycloalkylene or heterocyclylene radical; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-2; and

R^{16} is a hydrogen radical;

wherein each B is independently a
(1) bond;

(2) C_1-C_4 alkyl radical optionally substituted by (a) a radical of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, hydroxy or C_1-C_2 alkoxy, and/or (b) 1-2 halo radicals, and/or (c) a radical of heterocyclyl, aryl or heteroaryl optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_2 alkylsulfonylamino, hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthio, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals;

(3) heterocyclyl radical; or

(4) aryl or heteroaryl radical optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_2 alkylsulfonylamino, hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthio, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals;

each A is independently a

(1) hydrogen radical;

(2) halo radical;

(3) -C(O)-R^{30}, -C(O)-OR^{31}, -C(O)-$NR^{32}R^{31}$ or -C(NR^{32})-$NR^{32}R^{31}$ radical;

(4) -OR^{31} radical;

(5) -SR^{31}, -S(O)$_2$-R^{30} or -S(O)$_2$-$NR^{32}R^{31}$ radical; or

(6) -$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-S(O)$_2$-R^{30} or -NR^{33}-S(O)$_2$-$NR^{32}R^{31}$ radical;

wherein each R^{30} is independently

(1) -CF_3 or C_1-C_4 alkyl radical optionally substituted by 1-2 radicals of -CO_2R^{34}, amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4

alkoxy)carbonylamino, N-((C_1-C_4 alkoxy)carbonyl)-N-(C_1-C_4 alkyl)amino, hydroxy, C_1-C_4 alkoxy, aryl-C_1-C_2-alkoxy, heterocyclyl, aryl or heteroaryl radicals, wherein the heterocyclyl, aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_5 alkanoyl, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

(2) cycloalkyl or heterocyclyl radical optionally substituted by 1-2 radicals of (C_1-C_4 alkoxy)carbonyl, hydroxy or C_1-C_4 alkyl; or

(3) aryl or heteroaryl radicals optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

each R^{31} is independently hydrogen radical or R^{30}; and

wherein cycloalkyl is a monocyclic carbocyclic alkyl radical of 3-6 ring members, which is optionally partially unsaturated or benzo-fused; cycloalkylene is a monocyclic cycloalkyl gem divalent radical of 3-6 ring members; heterocyclyl is a radical of a monocyclic saturated heterocyclic ring system having 5-8 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally partially unsaturated or benzo-fused and optionally substituted by 1-2 oxo or thioxo radicals; heterocyclylene is a monocyclic heterocyclyl gem divalent radical on a ring carbon atom and having 5-6 ring members; aryl is a phenyl, biphenyl or naphthyl radical; and heteroaryl is radical of a monocyclic or bicyclic aromatic heterocyclic ring system having 5-6 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is

optionally benzo-fused or saturated C_3-C_4-carbocyclic-fused.

22. The compound of Claim 21 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_1-C_{12} alkyl or cycloalkyl radical optionally substituted by 1-2 radicals of -OH, $-OR^3$, $-NR^3R^4$, aryl, heteroaryl or cycloalkyl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl and cycloalkyl radicals are optionally substituted by 1-2 radicals of hydroxy, $-OR^3$, $-SR^3$, $-S(O)_2R^3$, $-NR^3R^4$, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, halo, C_1-C_6 alkyl or $-CF_3$ radicals; provided that the total number of aryl, heteroaryl and cycloalkyl radicals in R^1 is 0-2;

wherein each R^3 is independently an C_1-C_4 alkyl, $-CF_3$, aryl, heteroaryl, aryl-C_1-C_2-alkyl or heteroaryl-C_1-C_2-alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, methylsulfonylamino, C_1-C_2 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, halo, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$;

V is $-CHR^{11}-CHR^{12}-$; wherein R^{11} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{12} is (1) a hydrogen, $-OR^{20}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8

alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, aryloxy, heteroaryloxy, C_1-C_2 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals; or wherein R^{12} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{11} is (1) a hydrogen, $-OR^{20}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, aryloxy, heteroaryloxy, C_1-C_2 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals;

wherein each R^{20} is independently a hydrogen, C_1-C_4 alkyl-$C(O)R^{22}$, C_2-C_4 alkenyl, cycloalkyl, aryl, heteroaryl, aryl-C_1-C_2-alkyl, heteroaryl-C_1-C_2-alkyl or C_1-C_4 alkanoyl radical; wherein the cycloalkyl, aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

each R^{21} is independently an C_1-C_4 alkyl, C_1-C_4 alkyl-$C(O)R^{22}$, aryl, heteroaryl, aryl-C_1-C_2-alkyl or heteroaryl-C_1-C_2-alkyl radical; wherein the aryl and

heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals;

wherein each R^{22} is independently a hydroxy or $-NR^{23}R^{24}$ radical; wherein R^{23} is a hydrogen, C_1-C_2 alkyl, aryl, aryl-C_1-C_2-alkyl, heteroaryl or heteroaryl-C_1-C_2-alkyl radical; and R^{24} is a hydrogen or C_1-C_2 alkyl radical; or $-NR^{23}R^{24}$ represents a heteroaryl radical; wherein the aryl and heteroaryl radicals of R^{22}, R^{23} and $-NR^{23}R^{24}$ are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

W-N represents $-CR^{15}R^{16}$-N; wherein R^{15} is (1) a hydrogen, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl, radical optionally substituted with an $-OR^{20}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, C_1-C_4 alkoxycarbonylamino, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-2; and

R^{16} is a hydrogen radical;

wherein R^9 is independently -B-A; and
wherein R^{10} is independently -B-A when R^{11} and R^{12} are each independently a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical; and when R^{11} or R^{12} is independently other than a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4

alkyl radical, then R^{10} is independently a radical of hydrogen, halo, C_1-C_2 alkoxy, -CF_3 or C_1-C_4 alkyl optionally substituted by hydroxy or C_1-C_2 alkoxy radical; and provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^9 and R^{10} is 0-3;

wherein each B is independently a
(1) bond;
(2) C_1-C_4 alkyl radical; or
(3) aryl or heteroaryl radical optionally substituted by a radical of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_2 alkylsulfonylamino, hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthio, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals;

each A is independently a
(1) hydrogen radical;
(2) halo radical;
(3) -C(O)-R^{30}, -C(O)-OR^{31}, -C(O)-$NR^{32}R^{31}$ or -C(NR^{32})-$NR^{32}R^{31}$ radical;
(4) -OR^{31} radical;
(5) -SR^{31}, -S(O)$_2$-R^{30} or -S(O)$_2$-$NR^{32}R^{31}$ radical; or
(6) -$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31} or -NR^{33}-S(O)$_2$-R^{30} radical;

wherein each R^{30} is independently
(1) heterocyclyl radical optionally substituted by 1-2 radicals of (C_1-C_4 alkoxy)carbonyl, hydroxy or C_1-C_4 alkyl; or
(2) heteroaryl radicals optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals; and

each R^{31} is independently

(1) hydrogen or $-CF_3$ radical;

(2) C_1-C_4 alkyl radical optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy or aryl-C_1-C_2-alkoxy, aryl or heteroaryl radicals, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_5 alkanoyl, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

(3) cycloalkyl radical optionally substituted by 1-2 radicals of hydroxy or C_1-C_4 alkyl; or

(4) aryl or heteroaryl radicals optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals.

23. The compound of Claim 22 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_5-C_{12} alkyl radical optionally substituted by 1-2 radicals of $-OH$, $-OR^3$ or $-NR^3R^4$; or (2) aryl or heteroaryl radicals optionally substituted by a hydroxy, $-OR^3$, $-SR^3$, $-S(O)_2R^3$, $-NR^3R^4$, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, halo, C_1-C_6 alkyl or $-CF_3$ radicals; provided that the total number of aryl, heteroaryl and cycloalkyl radicals in R^1 is 0-1;

wherein each R^3 is independently an C_1-C_4 alkyl, -CF_3, aryl, heteroaryl, arylmethyl or heteroarylmethyl radical;

V is -CHR^{11}-CHR^{12}-; wherein R^{11} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{12} is (1) a hydrogen, -OR^{20}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-$S(O)_2$-R^{30}, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an -OR^{20}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-$S(O)_2$-R^{30}, aryl or heteroaryl radical; or wherein R^{12} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{11} is (1) a hydrogen, -OR^{20}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-$S(O)_2$-R^{30}, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an -OR^{20}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-$S(O)_2$-R^{30}, aryl or heteroaryl radical;

wherein each R^{20} is independently a hydrogen, C_2-C_4 alkenyl, cycloalkyl, aryl, heteroaryl, aryl-C_1-C_2-alkyl, heteroaryl-C_1-C_2-alkyl or C_1-C_4 alkanoyl radical; and

W-N represents -$CR^{15}R^{16}$-N; wherein R^{15} is (1) a hydrogen, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl, radical optionally substituted with an aryl or heteroaryl radical; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-2; and

X is S, Y is CR^{9} and Z is CR^{10};

wherein R^{9} is independently -B-A; and wherein R^{10} is independently -B-A when R^{11} and R^{12} are each independently a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical; and when R^{11} or R^{12} is independently other than a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical, then R^{10} is independently a radical of hydrogen, halo, C_1-C_2 alkoxy, $-CF_3$ or methyl radical; and provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^{9} and R^{10} is 0-3;

wherein each B is independently a
(1) bond;
(2) C_1-C_4 alkyl radical; or
(3) aryl or heteroaryl radical;

each A is independently a
(1) hydrogen radical;
(2) halo radical; or
(3) $-C(O)-R^{30}$, $-C(O)-OR^{31}$ or $-C(O)-NR^{32}R^{31}$ radical;

wherein each R^{30} is independently
(1) heterocyclyl radical optionally substituted by C_1-C_4 alkyl;

each R^{31} is independently hydrogen radical or
(1) C_1-C_4 alkyl radical optionally substituted by 1-2 radicals of aryl or heteroaryl radicals, wherein the aryl and heteroaryl radicals are optionally substituted

by a hydroxy, C_1-C_4 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; or
(2) cycloalkyl radical optionally substituted by 1-2 radicals of hydroxy or C_1-C_4 alkyl; or
(3) aryl or heteroaryl radicals optionally substituted by a hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

wherein heterocyclyl is a radical of pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiamorpholinyl, 4-benzyl-piperazin-1-yl, pyrimidinyl, tetrahydrofuryl, pyrazolidonyl, pyrazolinyl, pyridazinonyl, pyrrolidonyl, tetrahydrothienyl or its sulfoxide or sulfone derivative, 2,3-dihydroindolyl, tetrahydroquinolinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydro-1-oxo-isoquinolinyl, 2,3-dihydrobenzofuryl, benzopyranyl, methylenedioxyphenyl or ethylenedioxyphenyl; aryl is a phenyl, biphenyl or naphthyl radical; and heteroaryl is radical of imidazolyl, pyrrolyl, pyrazolyl, pyridyl, pyrazinyl, triazolyl, furyl, thienyl, oxazolyl, thiazolyl, indolyl, quinolinyl, isoquinolinyl, 5,6,7,8-tetrahydroquinolyl, 5,6,7,8-tetrahydroisoquinolinyl, quinoxalinyl, benzothiazolyl, ß-carbolinyl, benzofuryl, benzimidazolyl or benzoxazolyl.

24. The compound of Claim 3 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_1-C_{12} alkyl or cycloalkyl radical optionally substituted by 1-3 radicals of -OH, $-OR^3$, $-SR^3$, $-S(O)R^3$, $-S(O)_2R^3$, $-C(O)R^3$, $-NR^3R^4$, aryl, heteroaryl, cycloalkyl or heterocyclyl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl, cycloalkyl and heterocyclyl radicals are optionally substituted by 1-3

radicals of hydroxy, $-OR^3$, $-SR^3$, $-S(O)R^3$, $-S(O)_2R^3$, $-C(O)R^3$, $-NR^3R^4$, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_6 alkyl or $-CF_3$ radicals; provided that the total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^1 is 0-3; and each R^4 is independently a hydrogen or methyl radical;

wherein each R^3 is independently an C_1-C_4 alkyl, $-CF_3$, aryl, heteroaryl, aryl-C_1-C_4-alkyl or heteroaryl-C_1-C_4-alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$;

R^2 is a hydrogen radical;

V is $-CHR^{11}-$ or $-CHR^{11}-CHR^{12}-$; wherein R^{11} and R^{12} are each independently (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-

C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals;

wherein each R^{20} is independently a hydrogen, C_1-C_4 alkyl, C_2-C_4 alkenyl, cycloalkyl, aryl, heteroaryl, aryl-C_1-C_4-alkyl, heteroaryl-C_1-C_4-alkyl, C_1-C_4 alkanoyl, aroyl or heteroaroyl radical; wherein the alkyl and alkenyl radicals are optionally substituted by -C(O)R^{22}; and wherein the cycloalkyl, aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals; and

each R^{21} is independently an C_1-C_4 alkyl, C_1-C_4 alkyl-C(O)R^{22}, aryl, heteroaryl, aryl-C_1-C_4-alkyl or heteroaryl-C_1-C_4-alkyl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals;

wherein each R^{22} is independently a hydroxy, C_1-C_4 alkoxy, aryloxy, aryl-C_1-C_2-alkoxy, heteroaryloxy, heteroaryl-C_1-C_2-alkoxy or -$NR^{23}R^{24}$ radical; wherein R^{23} is a hydrogen, C_1-C_4 alkyl, aryl, aryl-C_1-C_2-alkyl, heteroaryl or heteroaryl-C_1-C_2-alkyl radical; and R^{24} is a hydrogen or C_1-C_4 alkyl radical; or -$NR^{23}R^{24}$ represents a heterocyclyl or heteroaryl radical; wherein the heterocyclyl, aryl and heteroaryl radicals of R^{22}, R^{23}

and $-NR^{23}R^{24}$ are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

W-N represents $-C(O)-N$, $-C(O)-CR^{15}R^{16}-N$, $-CR^{15}R^{16}-N$ or $-CR^{17}R^{18}-CR^{15}R^{16}-N$; wherein R^{15} is (1) a hydrogen, $-C(O)R^{22}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-3; and

R^{16} and R^{18} are each a hydrogen radical;

R^{17} is (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally

substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; or one of $-CR^{15}R^{16}-$ or $-CR^{17}R^{18}-$ represent a cycloalkylene or heterocyclylene radical; and

Y is O or S, X is CR^8 and Z is CR^{10};

wherein R^8 and R^{10} are each independently -B-A, provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^8 and R^{10} is 0-3;

wherein each B is independently a
(1) bond;
(2) C_1-C_8 alkyl radical optionally substituted by (a) a radical of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, and/or (b) 1-3 halo radicals, and/or (c) 1-2 radicals of heterocyclyl, aryl or heteroaryl optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;
(3) heterocyclyl radical; or
(4) aryl or heteroaryl radical optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy,

C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

each A is independently a

(1) hydrogen radical;

(2) halo, cyano or nitro radical;

(3) $-C(O)-R^{30}$, $-C(O)-OR^{31}$, $-C(O)-NR^{32}R^{31}$ or $-C(NR^{32})-NR^{32}R^{31}$ radical;

(4) $-OR^{31}$, $-O-C(O)-R^{31}$ or $-O-C(O)-NR^{32}R^{31}$ radical;

(5) $-SR^{31}$, $-S(O)-R^{30}$, $-S(O)_2-R^{30}$ or $-S(O)_2-NR^{32}R^{31}$ radical; or

(6) $-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(NR^{32})-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$ or $-NR^{33}-S(O)_2-NR^{32}R^{31}$ radical;

wherein each R^{30} is independently

(1) C_1-C_6 alkyl radical optionally substituted by 1-3 radicals of $-CO_2R^{34}$, amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, N-((C_1-C_4 alkoxy)carbonyl)-N-(C_1-C_4 alkyl)amino, aminocarbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, cyano, halo or aryl-C_1-C_4-alkoxy, aryl-C_1-C_4-alkylthio, aryl-C_1-C_4-alkylsulfonyl, C_3-C_8 cycloalkyl, heterocyclyl, aryl or heteroaryl radicals, wherein the cycloalkyl, heterocyclyl, aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, C_1-C_5 alkanoyl, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio,

C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, cyano, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals;
(2) cycloalkyl or heterocyclyl radical optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, C_1-C_4 alkyl, C_1-C_2 haloalkyl of 1-3 halo radicals or -OCF_3; or
(3) aryl or heteroaryl radicals optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals;

each R^{31} is independently hydrogen radical or R^{30}; and

each R^{33} is independently a hydrogen or methyl radical.

25. The compound of Claim 24 or a pharmaceutically acceptable salt thereof, wherein

V is -CHR^{11}-; wherein R^{11} is (1) a hydrogen, -OR^{20}, -SR^{21}, -$C(O)R^{22}$, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-$S(O)_2$-R^{30}, -NR^{33}-$S(O)_2$-$NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an -OR^{20}, -SR^{21}, -$C(O)R^{22}$, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-$S(O)_2$-R^{30}, -NR^{33}-$S(O)_2$-$NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2

radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

wherein R^8 is independently -B-A; and

wherein R^{10} is independently -B-A when R^{11} is a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical; and when R^{11} is other than a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical, then R^{10} is independently a radical of hydrogen, halo, C_1-C_2 alkoxy, amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, amidino, amido, carboxy, or C_1-C_4 alkyl optionally substituted by amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, 1-3 halo radicals, amidino, amido or carboxy radical; and provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^8 and R^{10} is 0-3.

26. The compound of Claim 25 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_1-C_{12} alkyl or cycloalkyl radical optionally substituted by 1-3 radicals of -OH, $-OR^3$, $-SR^3$, $-S(O)_2R^3$, $-NR^3R^4$, aryl, heteroaryl, cycloalkyl or heterocyclyl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl, cycloalkyl and heterocyclyl radicals are optionally substituted by 1-3 radicals of hydroxy, $-OR^3$, $-SR^3$, $-S(O)_2R^3$, $-NR^3R^4$, amino,

acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_6 alkyl or $-CF_3$ radicals; provided that the total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^1 is 0-2;

wherein each R^3 is independently an C_1-C_4 alkyl, $-CF_3$, aryl, heteroaryl, aryl-C_1-C_2-alkyl or heteroaryl-C_1-C_2-alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$;

V is $-CHR^{11}-$; wherein R^{11} is (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, methylsulfonyl, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

wherein each R^{22} is independently a hydroxy, C_1-C_4 alkoxy, aryloxy, aryl-C_1-C_2-alkoxy, heteroaryloxy, heteroaryl-C_1-C_2-alkoxy or $-NR^{23}R^{24}$ radical; wherein R^{23} is a hydrogen, C_1-C_4 alkyl, aryl, aryl-C_1-C_2-alkyl,

heteroaryl or heteroaryl-C_1-C_2-alkyl radical; and R^{24} is a hydrogen or C_1-C_4 alkyl radical; or $-NR^{23}R^{24}$ represents a heterocyclyl or heteroaryl radical; wherein the heterocyclyl, aryl and heteroaryl radicals of R^{22}, R^{23} and $-NR^{23}R^{24}$ are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

W-N represents $-C(O)-CR^{15}R^{16}-N$, $-CR^{15}R^{16}-N$ or $-CR^{17}R^{18}-CR^{15}R^{16}-N$; wherein R^{15} is (1) a hydrogen, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl radical optionally substituted with an $-OR^{20}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, C_1-C_4 alkoxycarbonylamino, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-2; and

R^{17} is (1) a hydrogen, $-OR^{20}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl radical optionally substituted with an $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; or one of $-CR^{15}R^{16}-$ or $-CR^{17}R^{18}-$ represent a cycloalkylene or heterocyclylene radical; and

wherein R^8 is a radical of hydrogen, halo, C_1-C_2 alkoxy, amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, amidino, amido, carboxy, or C_1-C_4 alkyl optionally substituted by amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, 1-3 halo radicals, amidino, amido or carboxy radical; and

wherein R^{10} is independently -B-A when R^{11} is a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical; and when R^{11} is other than a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical, then R^{10} is independently a radical of hydrogen, halo, C_1-C_2 alkoxy, amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, amidino, amido, carboxy, or C_1-C_4 alkyl optionally substituted by amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, 1-3 halo radicals, amidino, amido or carboxy radical; and provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^{10} is 0-2;

wherein each B is independently a
(1) bond;
(2) C_1-C_4 alkyl radical optionally substituted by (a) a radical of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, hydroxy or C_1-C_2 alkoxy, and/or (b) 1-2 halo radicals, and/or (c) a radical of heterocyclyl, aryl or heteroaryl optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_2 alkylsulfonylamino, hydroxy,

C_1-C_2 alkoxy, C_1-C_2 alkylthio, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

(3) heterocyclyl radical; or

(4) aryl or heteroaryl radical optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_2 alkylsulfonylamino, hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthio, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

each A is independently a

(1) hydrogen radical;

(2) halo radical;

(3) $-C(O)-R^{30}$, $-C(O)-OR^{31}$, $-C(O)-NR^{32}R^{31}$ or $-C(NR^{32})-NR^{32}R^{31}$ radical;

(4) $-OR^{31}$ radical;

(5) $-SR^{31}$, $-S(O)_2-R^{30}$ or $-S(O)_2-NR^{32}R^{31}$ radical; or

(6) $-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$ or $-NR^{33}-S(O)_2-NR^{32}R^{31}$ radical;

wherein each R^{30} is independently

(1) $-CF_3$ or C_1-C_4 alkyl radical optionally substituted by 1-2 radicals of $-CO_2R^{34}$, amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, N-((C_1-C_4 alkoxy)carbonyl)-N-(C_1-C_4 alkyl)amino, hydroxy, C_1-C_4 alkoxy, aryl-C_1-C_2-alkoxy, heterocyclyl, aryl or heteroaryl radicals, wherein the heterocyclyl, aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_5 alkanoyl, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

(2) cycloalkyl or heterocyclyl radical optionally substituted by 1-2 radicals of (C_1-C_4 alkoxy)carbonyl, hydroxy or C_1-C_4 alkyl; or

(3) aryl or heteroaryl radicals optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

each R^{31} is independently hydrogen radical or R^{30}; and

wherein cycloalkyl is a monocyclic carbocyclic alkyl radical of 3-6 ring members, which is optionally partially unsaturated or benzo-fused; cycloalkylene is a monocyclic cycloalkyl gem divalent radical of 3-6 ring members; heterocyclyl is a radical of a monocyclic saturated heterocyclic ring system having 5-8 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally partially unsaturated or benzo-fused and optionally substituted by 1-2 oxo or thioxo radicals; heterocyclylene is a monocyclic heterocyclyl gem divalent radical on a ring carbon atom and having 5-6 ring members; aryl is a phenyl, biphenyl or naphthyl radical; and heteroaryl is radical of a monocyclic or bicyclic aromatic heterocyclic ring system having 5-6 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally benzo-fused or saturated C_3-C_4-carbocyclic-fused.

27. The compound of Claim 26 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_1-C_{12} alkyl or cycloalkyl radical optionally substituted by 1-2 radicals of $-OH$, $-OR^3$,

$-NR^3R^4$, aryl, heteroaryl or cycloalkyl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl and cycloalkyl radicals are optionally substituted by 1-2 radicals of hydroxy, $-OR^3$, $-SR^3$, $-S(O)_2R^3$, $-NR^3R^4$, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, halo, C_1-C_6 alkyl or $-CF_3$ radicals; provided that the total number of aryl, heteroaryl and cycloalkyl radicals in R^1 is 0-2;

wherein each R^3 is independently an C_1-C_4 alkyl, $-CF_3$, aryl, heteroaryl, aryl-C_1-C_2-alkyl or heteroaryl-C_1-C_2-alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, methylsulfonylamino, C_1-C_2 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, halo, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$;

V is $-CHR^{11}-$; wherein R^{11} is (1) a hydrogen, $-OR^{20}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, aryloxy, heteroaryloxy, C_1-C_2 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals;

wherein each R^{20} is independently a hydrogen, C_1-C_4 alkyl-C(O)R^{22}, C_2-C_4 alkenyl, cycloalkyl, aryl, heteroaryl, aryl-C_1-C_2-alkyl, heteroaryl-C_1-C_2-alkyl or C_1-C_4 alkanoyl radical; wherein the cycloalkyl, aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

each R^{21} is independently an C_1-C_4 alkyl, C_1-C_4 alkyl-C(O)R^{22}, aryl, heteroaryl, aryl-C_1-C_2-alkyl or heteroaryl-C_1-C_2-alkyl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals;

wherein each R^{22} is independently a hydroxy or $-NR^{23}R^{24}$ radical; wherein R^{23} is a hydrogen, C_1-C_2 alkyl, aryl, aryl-C_1-C_2-alkyl, heteroaryl or heteroaryl-C_1-C_2-alkyl radical; and R^{24} is a hydrogen or C_1-C_2 alkyl radical; or $-NR^{23}R^{24}$ represents a heteroaryl radical; wherein the aryl and heteroaryl radicals of R^{22}, R^{23} and $-NR^{23}R^{24}$ are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

W-N represents $-C(O)-CR^{15}R^{16}-N$, $-CR^{15}R^{16}-N$ or $-CR^{17}R^{18}-CR^{15}R^{16}-N$; wherein R^{15} is (1) a hydrogen, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl radical optionally substituted with an $-OR^{20}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, C_1-C_4

alkoxycarbonylamino, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-2; and

R^{16} and R^{18} are each a hydrogen radical;

R^{17} is (1) a hydrogen, $-OR^{20}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl radical optionally substituted with an $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

wherein R^8 is a radical of hydrogen, halo, C_1-C_2 alkoxy, $-CF_3$ or C_1-C_4 alkyl optionally substituted by hydroxy or C_1-C_2 alkoxy radical; and

wherein R^{10} is independently -B-A when R^{11} is a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical; and when R^{11} is other than a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical, then R^{10} is independently a radical of hydrogen, halo, C_1-C_2 alkoxy, $-CF_3$ or C_1-C_4 alkyl optionally substituted by hydroxy or C_1-C_2 alkoxy radical; and provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^{10} is 0-2;

wherein each B is independently a

(1) bond;
(2) C_1-C_4 alkyl radical; or
(3) aryl or heteroaryl radical optionally substituted by a radical of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_2 alkylsulfonylamino, hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthio, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

each A is independently a
(1) hydrogen radical;
(2) halo radical;
(3) $-C(O)-R^{30}$, $-C(O)-OR^{31}$, $-C(O)-NR^{32}R^{31}$ or $-C(NR^{32})-NR^{32}R^{31}$ radical;
(4) $-OR^{31}$ radical;
(5) $-SR^{31}$, $-S(O)_2-R^{30}$ or $-S(O)_2-NR^{32}R^{31}$ radical; or
(6) $-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$ or $-NR^{33}-S(O)_2-R^{30}$ radical;

wherein each R^{30} is independently
(1) heterocyclyl radical optionally substituted by 1-2 radicals of (C_1-C_4 alkoxy)carbonyl, hydroxy or C_1-C_4 alkyl; or
(2) heteroaryl radicals optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

each R^{31} is independently
(1) hydrogen or $-CF_3$ radical;
(2) C_1-C_4 alkyl radical optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy or aryl-C_1-C_2-alkoxy, aryl or heteroaryl radicals, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2

alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_5 alkanoyl, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

(3) cycloalkyl radical optionally substituted by 1-2 radicals of hydroxy or C_1-C_4 alkyl; or

(4) aryl or heteroaryl radicals optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals.

28. The compound of Claim 27 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_1-C_{12} alkyl or cycloalkyl radical optionally substituted by 1-2 radicals of -OH, $-OR^3$, $-NR^3R^4$, aryl or heteroaryl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl and cycloalkyl radicals are optionally substituted by 1-2 radicals of hydroxy, $-OR^3$, $-SR^3$, $-S(O)_2R^3$, $-NR^3R^4$, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, halo, C_1-C_6 alkyl or $-CF_3$ radicals; provided that the total number of aryl, heteroaryl and cycloalkyl radicals in R^1 is 0-1;

wherein each R^3 is independently an C_1-C_4 alkyl, $-CF_3$, aryl, heteroaryl, arylmethyl or heteroarylmethyl radical;

V is $-CHR^{11}-$; wherein R^{11} is (1) a hydrogen, $-OR^{20}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or

(2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical;

wherein each R^{20} is independently a hydrogen, C_2-C_4 alkenyl, cycloalkyl, aryl, heteroaryl, aryl-C_1-C_2-alkyl, heteroaryl-C_1-C_2-alkyl or C_1-C_4 alkanoyl radical; and

W-N represents $-C(O)-CR^{15}R^{16}-N$, $-CR^{15}R^{16}-N$ or $-CR^{17}R^{18}-CR^{15}R^{16}-N$; wherein R^{15} is (1) a hydrogen, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl radical optionally substituted with an aryl or heteroaryl radical; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-2; and

R^{17} is a hydrogen, hydroxy or C_1-C_4 alkyl radical; and

Y is S, X is CR^8 and Z is CR^{10};

wherein R^8 is a radical of hydrogen, halo, C_1-C_2 alkoxy, $-CF_3$ or methyl; and

wherein R^{10} is independently -B-A when R^{11} is a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical; and when R^{11} is other than a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical, then R^{10} is independently a radical of hydrogen, halo, C_1-C_2 alkoxy, $-CF_3$ or methyl radical; and provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^{10} is 0-2;

wherein each B is independently a
(1) bond;
(2) C_1-C_4 alkyl radical; or
(3) aryl or heteroaryl radical;

each A is independently a
(1) hydrogen radical;
(2) halo radical; or
(3) $-C(O)-R^{30}$, $-C(O)-OR^{31}$ or $-C(O)-NR^{32}R^{31}$ radical;

wherein each R^{30} is independently a heterocyclyl radical optionally substituted by C_1-C_4 alkyl; and

each R^{31} is independently hydrogen radical or
(1) C_1-C_4 alkyl radical optionally substituted by 1-2 radicals of aryl or heteroaryl radicals, wherein the aryl and heteroaryl radicals are optionally substituted by a hydroxy, C_1-C_4 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radical; or
(2) cycloalkyl radical optionally substituted by 1-2 radicals of hydroxy or C_1-C_4 alkyl; or
(3) aryl or heteroaryl radicals optionally substituted by a hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radical.

29. The compound of Claim 28 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_5-C_{12} alkyl radical optionally substituted by 1-2 radicals of -OH, $-OR^3$ or $-NR^3R^4$; or (2) aryl or heteroaryl radicals optionally substituted by a hydroxy, $-OR^3$, $-SR^3$, $-S(O)_2R^3$, $-NR^3R^4$, amino, acetylamino,

methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, halo, C_1-C_6 alkyl or -CF_3 radical; provided that the total number of aryl and heteroaryl radicals in R^1 is 0-1; and

wherein heterocyclyl is a radical of pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiamorpholinyl, 4-benzyl-piperazin-1-yl, pyrimidinyl, tetrahydrofuryl, pyrazolidonyl, pyrazolinyl, pyridazinonyl, pyrrolidonyl, tetrahydrothienyl or its sulfoxide or sulfone derivative, 2,3-dihydroindolyl, tetrahydroquinolinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydro-1-oxo-isoquinolinyl, 2,3-dihydrobenzofuryl, benzopyranyl, methylenedioxyphenyl or ethylenedioxyphenyl; aryl is a phenyl, biphenyl or naphthyl radical; and heteroaryl is radical of imidazolyl, pyrrolyl, pyrazolyl, pyridyl, pyrazinyl, triazolyl, furyl, thienyl, oxazolyl, thiazolyl, indolyl, quinolinyl, isoquinolinyl, 5,6,7,8-tetrahydroquinolyl, 5,6,7,8-tetrahydroisoquinolinyl, quinoxalinyl, benzothiazolyl, ß-carbolinyl, benzofuryl, benzimidazolyl or benzoxazolyl.

30. The compound of Claim 24 or a pharmaceutically acceptable salt thereof, wherein

V is -CHR^{11}-CHR^{12}-; wherein R^{11} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{12} is (1) a hydrogen, -OR^{20}, -SR^{21}, -C(O)R^{22}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-$S(O)_2$-R^{30}, -NR^{33}-$S(O)_2$-$NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an -OR^{20}, -SR^{21}, -C(O)R^{22}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$,

$-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; or wherein R^{12} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{11} is (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

W-N represents -C(O)-N or $-CR^{15}R^{16}-N$; wherein R^{15} is (1) a hydrogen, $-C(O)R^{22}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl,

methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-3; and

R^{16} is a hydrogen radical; or $-CR^{15}R^{16}-$ represents a cycloalkylene or heterocyclylene radical; and

wherein R^{8} is independently -B-A; and
wherein R^{10} is independently -B-A when R^{11} and R^{12} are each independently a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical; and when R^{11} or R^{12} is independently other than a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical, then R^{10} is independently a radical of hydrogen, halo, C_1-C_2 alkoxy, amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, amidino, amido, carboxy, or C_1-C_4 alkyl optionally substituted by amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, 1-3 halo radicals, amidino, amido or carboxy radical; and provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^{8} and R^{10} is 0-3.

31. The compound of Claim 30 or a pharmaceutically acceptable salt thereof, wherein

R^{1} is (1) an C_1-C_{12} alkyl or cycloalkyl radical optionally substituted by 1-3 radicals of -OH, $-OR^{3}$, $-SR^{3}$, $-S(O)_2R^{3}$, $-NR^{3}R^{4}$, aryl, heteroaryl, cycloalkyl or heterocyclyl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl, cycloalkyl and

heterocyclyl radicals are optionally substituted by 1-3 radicals of hydroxy, $-OR^3$, $-SR^3$, $-S(O)_2R^3$, $-NR^3R^4$, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_6 alkyl or $-CF_3$ radicals; provided that the total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^1 is 0-2;

wherein each R^3 is independently an C_1-C_4 alkyl, $-CF_3$, aryl, heteroaryl, aryl-C_1-C_2-alkyl or heteroaryl-C_1-C_2-alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$; and each R^4 is independently a hydrogen or methyl radical;

V is $-CHR^{11}-CHR^{12}-$; wherein R^{11} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{12} is (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, methylsulfonyl, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; or wherein R^{12} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{11} is

(1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, methylsulfonyl, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

wherein each R^{22} is independently a hydroxy, C_1-C_4 alkoxy, aryloxy, aryl-C_1-C_2-alkoxy, heteroaryloxy, heteroaryl-C_1-C_2-alkoxy or $-NR^{23}R^{24}$ radical; wherein R^{23} is a hydrogen, C_1-C_4 alkyl, aryl, aryl-C_1-C_2-alkyl, heteroaryl or heteroaryl-C_1-C_2-alkyl radical; and R^{24} is a hydrogen or C_1-C_4 alkyl radical; or $-NR^{23}R^{24}$ represents a heterocyclyl or heteroaryl radical; wherein the heterocyclyl, aryl and heteroaryl radicals of R^{22}, R^{23} and $-NR^{23}R^{24}$ are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

W-N represents $-CR^{15}R^{16}-N$; wherein R^{15} is (1) a hydrogen, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl radical optionally substituted with an $-OR^{20}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, C_1-C_4 alkoxycarbonylamino, halo, C_1-C_4

alkyl, $-CF_3$ or $-OCF_3$ radicals; or $-CR^{15}R^{16}-$ represents a cycloalkylene or heterocyclylene radical; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-2; and

R^{16} is a hydrogen radical;

wherein R^8 is a radical of hydrogen, halo, C_1-C_2 alkoxy, amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, amidino, amido, carboxy, or C_1-C_4 alkyl optionally substituted by amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, 1-3 halo radicals, amidino, amido or carboxy radical; and

wherein R^{10} is independently -B-A when R^{11} and R^{12} are each independently a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical; and when R^{11} or R^{12} is independently other than a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical, then R^{10} is independently a radical of hydrogen, halo, C_1-C_2 alkoxy, amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, amidino, amido, carboxy, or C_1-C_4 alkyl optionally substituted by amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, 1-3 halo radicals, amidino, amido or carboxy radical; and provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^{10} is 0-2;

wherein each B is independently a
(1) bond;
(2) C_1-C_4 alkyl radical optionally substituted by (a) a radical of amino, C_1-C_2 alkylamino, di-(C_1-C_2

alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, hydroxy or C_1-C_2 alkoxy, and/or (b) 1-2 halo radicals, and/or (c) a radical of heterocyclyl, aryl or heteroaryl optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_2 alkylsulfonylamino, hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthio, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals;

(3) heterocyclyl radical; or

(4) aryl or heteroaryl radical optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_2 alkylsulfonylamino, hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthio, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals;

each A is independently a

(1) hydrogen radical;

(2) halo radical;

(3) -C(O)-R^{30}, -C(O)-OR^{31}, -C(O)-$NR^{32}R^{31}$ or -C(NR^{32})-$NR^{32}R^{31}$ radical;

(4) -OR^{31} radical;

(5) -SR^{31}, -S$(O)_2$-R^{30} or -S$(O)_2$-$NR^{32}R^{31}$ radical; or

(6) -$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-S$(O)_2$-R^{30} or -NR^{33}-S$(O)_2$-$NR^{32}R^{31}$ radical;

wherein each R^{30} is independently

(1) -CF_3 or C_1-C_4 alkyl radical optionally substituted by 1-2 radicals of -CO_2R^{34}, amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, N-((C_1-C_4 alkoxy)carbonyl)-N-(C_1-C_4 alkyl)amino, hydroxy, C_1-C_4 alkoxy, aryl-C_1-C_2-alkoxy,

heterocyclyl, aryl or heteroaryl radicals, wherein the heterocyclyl, aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_5 alkanoyl, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

(2) cycloalkyl or heterocyclyl radical optionally substituted by 1-2 radicals of (C_1-C_4 alkoxy)carbonyl, hydroxy or C_1-C_4 alkyl; or

(3) aryl or heteroaryl radicals optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

each R^{31} is independently hydrogen radical or R^{30}; and

wherein cycloalkyl is a monocyclic carbocyclic alkyl radical of 3-6 ring members, which is optionally partially unsaturated or benzo-fused; cycloalkylene is a monocyclic cycloalkyl gem divalent radical of 3-6 ring members; heterocyclyl is a radical of a monocyclic saturated heterocyclic ring system having 5-8 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally partially unsaturated or benzo-fused and optionally substituted by 1-2 oxo or thioxo radicals; heterocyclylene is a monocyclic heterocyclyl gem divalent radical on a ring carbon atom and having 5-6 ring members; aryl is a phenyl, biphenyl or naphthyl radical; and heteroaryl is radical of a monocyclic or bicyclic aromatic heterocyclic ring system having 5-6 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally benzo-fused or saturated C_3-C_4-carbocyclic-fused.

32. The compound of Claim 31 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_1-C_{12} alkyl or cycloalkyl radical optionally substituted by 1-2 radicals of -OH, -OR^3, -NR^3R^4, aryl, heteroaryl or cycloalkyl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl and cycloalkyl radicals are optionally substituted by 1-2 radicals of hydroxy, -OR^3, -SR^3, -$S(O)_2R^3$, -NR^3R^4, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, halo, C_1-C_6 alkyl or -CF_3 radicals; provided that the total number of aryl, heteroaryl and cycloalkyl radicals in R^1 is 0-2;

wherein each R^3 is independently an C_1-C_4 alkyl, -CF_3, aryl, heteroaryl, aryl-C_1-C_2-alkyl or heteroaryl-C_1-C_2-alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, methylsulfonylamino, C_1-C_2 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, halo, C_1-C_2 alkyl, -CF_3 or -OCF_3; and each R^4 is independently a hydrogen or methyl radical;

V is -CHR^{11}-CHR^{12}-; wherein R^{11} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{12} is (1) a hydrogen, -OR^{20}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-$S(O)_2$-R^{30}, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8

alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, aryloxy, heteroaryloxy, C_1-C_2 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals; or wherein R^{12} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{11} is (1) a hydrogen, $-OR^{20}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, aryloxy, heteroaryloxy, C_1-C_2 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals;

wherein each R^{20} is independently a hydrogen, C_1-C_4 alkyl-$C(O)R^{22}$, C_2-C_4 alkenyl, cycloalkyl, aryl, heteroaryl, aryl-C_1-C_2-alkyl, heteroaryl-C_1-C_2-alkyl or C_1-C_4 alkanoyl radical; wherein the cycloalkyl, aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

each R^{21} is independently an C_1-C_4 alkyl, C_1-C_4 alkyl-$C(O)R^{22}$, aryl, heteroaryl, aryl-C_1-C_2-alkyl or heteroaryl-C_1-C_2-alkyl radical; wherein the aryl and

heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals;

wherein each R^{22} is independently a hydroxy or $-NR^{23}R^{24}$ radical; wherein R^{23} is a hydrogen, C_1-C_2 alkyl, aryl, aryl-C_1-C_2-alkyl, heteroaryl or heteroaryl-C_1-C_2-alkyl radical; and R^{24} is a hydrogen or C_1-C_2 alkyl radical; or $-NR^{23}R^{24}$ represents a heteroaryl radical; wherein the aryl and heteroaryl radicals of R^{22}, R^{23} and $-NR^{23}R^{24}$ are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

W-N represents $-CR^{15}R^{16}$-N; wherein R^{15} is (1) a hydrogen, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl, radical optionally substituted with an $-OR^{20}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, C_1-C_4 alkoxycarbonylamino, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-2; and

R^{16} is a hydrogen radical;

wherein R^8 is a radical of hydrogen, halo, C_1-C_2 alkoxy, $-CF_3$ or C_1-C_4 alkyl optionally substituted by hydroxy or C_1-C_2 alkoxy radical; and

wherein R^{10} is independently -B-A when R^{11} and R^{12} are each independently a hydrogen, hydroxy, C_1-C_2 alkoxy or

C_1-C_4 alkyl radical; and when R^{11} or R^{12} is independently other than a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical, then R^{10} is independently a radical of hydrogen, halo, C_1-C_2 alkoxy, $-CF_3$ or C_1-C_4 alkyl optionally substituted by hydroxy or C_1-C_2 alkoxy radical; and provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^{10} is 0-2;

wherein each B is independently a
(1) bond;
(2) C_1-C_4 alkyl radical; or
(3) aryl or heteroaryl radical optionally substituted by a radical of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_2 alkylsulfonylamino, hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthio, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

each A is independently a
(1) hydrogen radical;
(2) halo radical;
(3) $-C(O)-R^{30}$, $-C(O)-OR^{31}$, $-C(O)-NR^{32}R^{31}$ or $-C(NR^{32})-NR^{32}R^{31}$ radical;
(4) $-OR^{31}$ radical;
(5) $-SR^{31}$, $-S(O)_2-R^{30}$ or $-S(O)_2-NR^{32}R^{31}$ radical; or
(6) $-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$ or $-NR^{33}-S(O)_2-R^{30}$ radical;

wherein each R^{30} is independently
(1) heterocyclyl radical optionally substituted by 1-2 radicals of (C_1-C_4 alkoxy)carbonyl, hydroxy or C_1-C_4 alkyl; or

(2) heteroaryl radicals optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

each R^{31} is independently

(1) hydrogen or $-CF_3$ radical;

(2) C_1-C_4 alkyl radical optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy or aryl-C_1-C_2-alkoxy, aryl or heteroaryl radicals, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_5 alkanoyl, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

(3) cycloalkyl radical optionally substituted by 1-2 radicals of hydroxy or C_1-C_4 alkyl; or

(4) aryl or heteroaryl radicals optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals.

33. The compound of Claim 32 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_5-C_{12} alkyl radical optionally substituted by 1-2 radicals of -OH, $-OR^3$ or $-NR^3R^4$; or (2) aryl or heteroaryl radicals optionally substituted by a hydroxy, $-OR^3$, $-SR^3$, $-S(O)_2R^3$, $-NR^3R^4$, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, halo, C_1-C_6 alkyl or $-CF_3$ radicals;

provided that the total number of aryl, heteroaryl and cycloalkyl radicals in R^1 is 0-1;

wherein each R^3 is independently an C_1-C_4 alkyl, $-CF_3$, aryl, heteroaryl, arylmethyl or heteroarylmethyl radical; and each R^4 is independently a hydrogen or methyl radical;

V is $-CHR^{11}-CHR^{12}-$; wherein R^{11} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{12} is (1) a hydrogen, $-OR^{20}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or wherein R^{12} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{11} is (1) a hydrogen, $-OR^{20}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical;

wherein each R^{20} is independently a hydrogen, C_2-C_4 alkenyl, cycloalkyl, aryl, heteroaryl, aryl-C_1-C_2-alkyl, heteroaryl-C_1-C_2-alkyl or C_1-C_4 alkanoyl radical; and

W-N represents $-CR^{15}R^{16}-N$; wherein R^{15} is (1) a hydrogen, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl, radical optionally substituted with an aryl or heteroaryl radical; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-2; and

Y is S, X is CR^8 and Z is CR^{10};

wherein R^8 is a radical of hydrogen, halo, C_1-C_2 alkoxy, $-CF_3$ or methyl; and

wherein R^{10} is independently -B-A when R^{11} and R^{12} are each independently a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical; and when R^{11} or R^{12} is independently other than a hydrogen, hydroxy, C_1-C_2 alkoxy or C_1-C_4 alkyl radical, then R^{10} is independently a radical of hydrogen, halo, C_1-C_2 alkoxy, $-CF_3$ or methyl radical; and provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^{10} is 0-2;

wherein each B is independently a
(1) bond;
(2) C_1-C_4 alkyl radical;
(3) aryl or heteroaryl radical;

each A is independently a
(1) hydrogen radical;
(2) halo radical; or
(3) $-C(O)-R^{30}$, $-C(O)-OR^{31}$ or $-C(O)-NR^{32}R^{31}$ radical;

wherein each R^{30} is independently heterocyclyl radical optionally substituted by C_1-C_4 alkyl;

each R^{31} is independently hydrogen radical or (1) C_1-C_4 alkyl radical optionally substituted by 1-2 radicals of aryl or heteroaryl radicals, wherein the aryl and heteroaryl radicals are optionally substituted by a hydroxy, C_1-C_4 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; or

(2) cycloalkyl radical optionally substituted by 1-2 radicals of hydroxy or C_1-C_4 alkyl; or

(3) aryl or heteroaryl radicals optionally substituted by a hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

wherein heterocyclyl is a radical of pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiamorpholinyl, 4-benzyl-piperazin-1-yl, pyrimidinyl, tetrahydrofuryl, pyrazolidonyl, pyrazolinyl, pyridazinonyl, pyrrolidonyl, tetrahydrothienyl or its sulfoxide or sulfone derivative, 2,3-dihydroindolyl, tetrahydroquinolinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydro-1-oxo-isoquinolinyl, 2,3-dihydrobenzofuryl, benzopyranyl, methylenedioxyphenyl or ethylenedioxyphenyl; aryl is a phenyl, biphenyl or naphthyl radical; and heteroaryl is radical of imidazolyl, pyrrolyl, pyrazolyl, pyridyl, pyrazinyl, triazolyl, furyl, thienyl, oxazolyl, thiazolyl, indolyl, quinolinyl, isoquinolinyl, 5,6,7,8-tetrahydroquinolyl, 5,6,7,8-tetrahydroisoquinolinyl, quinoxalinyl, benzothiazolyl, ß-carbolinyl, benzofuryl, benzimidazolyl or benzoxazolyl.

34. The compound of Claim 3 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_1-C_{12} alkyl or cycloalkyl radical optionally substituted by 1-3 radicals of -OH, -OR^3, -SR^3, -S(O)R^3, -S(O)$_2R^3$, -C(O)R^3, -NR^3R^4, aryl, heteroaryl, cycloalkyl or heterocyclyl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl, cycloalkyl and heterocyclyl radicals are optionally substituted by 1-3 radicals of hydroxy, -OR^3, -SR^3, -S(O)R^3, -S(O)$_2R^3$, -C(O)R^3, -NR^3R^4, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_6 alkyl or -CF_3 radicals; provided that the total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^1 is 0-3;

wherein each R^3 is independently an C_1-C_4 alkyl, -CF_3, aryl, heteroaryl, aryl-C_1-C_4-alkyl or heteroaryl-C_1-C_4-alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3; and each R^4 is independently a hydrogen or methyl radical;

R^2 is a hydrogen radical;

V is -CHR^{11}- or -CHR^{11}-CHR^{12}-; wherein R^{11} and R^{12} are each independently (1) a hydrogen, -OR^{20}, -SR^{21}, -C(O)R^{22}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-S(O)$_2$-R^{30}, -NR^{33}-S(O)$_2$-$NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted with an -OR^{20}, -SR^{21}, -C(O)R^{22}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -

NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-S$(O)_2$-R^{30}, -NR^{33}-S$(O)_2$-$NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals;

wherein each R^{20} is independently a hydrogen, C_1-C_4 alkyl, C_2-C_4 alkenyl, cycloalkyl, aryl, heteroaryl, aryl-C_1-C_4-alkyl, heteroaryl-C_1-C_4-alkyl, C_1-C_4 alkanoyl, aroyl or heteroaroyl radical; wherein the alkyl and alkenyl radicals are optionally substituted by -C(O)R^{22}; and wherein the cycloalkyl, aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals; and

each R^{21} is independently an C_1-C_4 alkyl, C_1-C_4 alkyl-C(O)R^{22}, aryl, heteroaryl, aryl-C_1-C_4-alkyl or heteroaryl-C_1-C_4-alkyl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals;

wherein each R^{22} is independently a hydroxy, C_1-C_4 alkoxy, aryloxy, aryl-C_1-C_2-alkoxy, heteroaryloxy,

heteroaryl-C_1-C_2-alkoxy or -$NR^{23}R^{24}$ radical; wherein R^{23} is a hydrogen, C_1-C_4 alkyl, aryl, aryl-C_1-C_2-alkyl, heteroaryl or heteroaryl-C_1-C_2-alkyl radical; and R^{24} is a hydrogen or C_1-C_4 alkyl radical; or -$NR^{23}R^{24}$ represents a heterocyclyl or heteroaryl radical; wherein the heterocyclyl, aryl and heteroaryl radicals of R^{22}, R^{23} and -$NR^{23}R^{24}$ are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals; and

W-N represents -C(O)-N, -C(O)-$CR^{15}R^{16}$-N, -$CR^{15}R^{16}$-N or -$CR^{17}R^{18}$-$CR^{15}R^{16}$-N; wherein R^{15} is (1) a hydrogen, -C(O)R^{22}, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted with an -OR^{20}, -SR^{21}, -C(O)R^{22}, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-3; and

R^{16} and R^{18} are each a hydrogen radical;

R^{17} is (1) a hydrogen, -OR^{20}, -SR^{21}, -C(O)R^{22}, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-S(O)$_2$-R^{30}, -

NR^{33}-$S(O)_2$-$NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted with an -OR^{20}, -SR^{21}, -$C(O)R^{22}$, -NR^{33}-$C(O)$-R^{31}, -NR^{33}-$C(O)$-OR^{30}, -NR^{33}-$C(O)$-$NR^{32}R^{31}$, -NR^{33}-$S(O)_2$-R^{30}, -NR^{33}-$S(O)_2$-$NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals; or one of -$CR^{15}R^{16}$- or -$CR^{17}R^{18}$- represent a cycloalkylene or heterocyclylene radical; and

X is O or S, Y is CR^9 and Z is N; or Z is O or S, X is N and Y is CR^9;

wherein R^9 is -B-A, provided that the total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^9 is 0-2;

wherein each B is independently a
(1) bond;
(2) C_1-C_8 alkyl radical optionally substituted by (a) a radical of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, and/or (b) 1-3 halo radicals, and/or (c) 1-2 radicals of heterocyclyl, aryl or heteroaryl optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy,

C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals;

(3) heterocyclyl radical; or

(4) aryl or heteroaryl radical optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals;

each A is independently a

(1) hydrogen radical;

(2) halo, cyano or nitro radical;

(3) -C(O)-R^{30}, -C(O)-OR^{31}, -C(O)-$NR^{32}R^{31}$ or -C(NR^{32})-$NR^{32}R^{31}$ radical;

(4) -OR^{31}, -O-C(O)-R^{31} or -O-C(O)-$NR^{32}R^{31}$ radical;

(5) -SR^{31}, -S(O)-R^{30}, -$S(O)_2$-R^{30} or -$S(O)_2$-$NR^{32}R^{31}$ radical; or

(6) -$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(NR^{32})-$NR^{32}R^{31}$, -NR^{33}-$S(O)_2$-R^{30} or -NR^{33}-$S(O)_2$-$NR^{32}R^{31}$ radical;

wherein each R^{30} is independently

(1) C_1-C_6 alkyl radical optionally substituted by 1-3 radicals of -CO_2R^{34}, amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, N-((C_1-C_4 alkoxy)carbonyl)-N-(C_1-C_4 alkyl)amino, aminocarbonylamino, C_1-C_4 alkylsulfonylamino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, cyano, halo or aryl-C_1-C_4-alkoxy, aryl-C_1-C_4-alkylthio, aryl-C_1-C_4-alkylsulfonyl, C_3-C_8 cycloalkyl, heterocyclyl, aryl or heteroaryl radicals, wherein the

cycloalkyl, heterocyclyl, aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, C_1-C_5 alkanoyl, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, C_1-C_4 alkylsulfinyl, C_1-C_4 alkylsulfonyl, cyano, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals;

(2) cycloalkyl or heterocyclyl radical optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, C_1-C_4 alkyl, C_1-C_2 haloalkyl of 1-3 halo radicals or -OCF_3; or

(3) aryl or heteroaryl radicals optionally substituted by 1-3 radicals of amino, C_1-C_4 alkylamino, di-(C_1-C_4 alkyl)amino, C_1-C_5 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_4 alkylsulfonylamino, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, cyano, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals;

each R^{31} is independently hydrogen radical or R^{30}; and

each R^{33} is independently a hydrogen or methyl radical.

35. The compound of Claim 34 or a pharmaceutically acceptable salt thereof, wherein

V is -CHR^{11}-; wherein R^{11} is (1) a hydrogen, -OR^{20}, -SR^{21}, -$C(O)R^{22}$, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-$S(O)_2$-R^{30}, -NR^{33}-$S(O)_2$-$NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-

C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals.

36. The compound of Claim 35 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_1-C_{12} alkyl or cycloalkyl radical optionally substituted by 1-3 radicals of -OH, $-OR^3$, $-SR^3$, $-S(O)_2R^3$, $-NR^3R^4$, aryl, heteroaryl, cycloalkyl or heterocyclyl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl, cycloalkyl and heterocyclyl radicals are optionally substituted by 1-3 radicals of hydroxy, $-OR^3$, $-SR^3$, $-S(O)_2R^3$, $-NR^3R^4$, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_6 alkyl or $-CF_3$ radicals; provided that the total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^1 is 0-2;

wherein each R^3 is independently an C_1-C_4 alkyl, $-CF_3$, aryl, heteroaryl, aryl-C_1-C_2-alkyl or heteroaryl-C_1-C_2-alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino,

methylsulfonylamino, C_1-C_4 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$;

V is $-CHR^{11}-$; wherein R^{11} is (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, methylsulfonyl, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

wherein each R^{22} is independently a hydroxy, C_1-C_4 alkoxy, aryloxy, aryl-C_1-C_2-alkoxy, heteroaryloxy, heteroaryl-C_1-C_2-alkoxy or $-NR^{23}R^{24}$ radical; wherein R^{23} is a hydrogen, C_1-C_4 alkyl, aryl, aryl-C_1-C_2-alkyl, heteroaryl or heteroaryl-C_1-C_2-alkyl radical; and R^{24} is a hydrogen or C_1-C_4 alkyl radical; or $-NR^{23}R^{24}$ represents a heterocyclyl or heteroaryl radical; wherein the heterocyclyl, aryl and heteroaryl radicals of R^{22}, R^{23} and $-NR^{23}R^{24}$ are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

W-N represents $-C(O)-CR^{15}R^{16}-N$, $-CR^{15}R^{16}-N$ or $-CR^{17}R^{18}-CR^{15}R^{16}-N$; wherein R^{15} is (1) a hydrogen, aryl or

heteroaryl radical; or (2) an C_1-C_4 alkyl radical optionally substituted with an $-OR^{20}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, C_1-C_4 alkoxycarbonylamino, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-2; and

R^{17} is (1) a hydrogen, $-OR^{20}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl radical optionally substituted with an $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; or one of $-CR^{15}R^{16}-$ or $-CR^{17}R^{18}-$ represent a cycloalkylene or heterocyclylene radical; and

wherein each B is independently a
(1) bond;
(2) C_1-C_4 alkyl radical optionally substituted by (a) a radical of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, hydroxy or C_1-C_2 alkoxy, and/or (b) 1-2 halo radicals, and/or (c) a radical of heterocyclyl, aryl or heteroaryl optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_2 alkylsulfonylamino, hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthio, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

(3) heterocyclyl radical; or

(4) aryl or heteroaryl radical optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_2 alkylsulfonylamino, hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthio, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

each A is independently a

(1) hydrogen radical;

(2) halo radical;

(3) $-C(O)-R^{30}$, $-C(O)-OR^{31}$, $-C(O)-NR^{32}R^{31}$ or $-C(NR^{32})-NR^{32}R^{31}$ radical;

(4) $-OR^{31}$ radical;

(5) $-SR^{31}$, $-S(O)_2-R^{30}$ or $-S(O)_2-NR^{32}R^{31}$ radical; or

(6) $-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$ or $-NR^{33}-S(O)_2-NR^{32}R^{31}$ radical;

wherein each R^{30} is independently

(1) $-CF_3$ or C_1-C_4 alkyl radical optionally substituted by 1-2 radicals of $-CO_2R^{34}$, amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, N-((C_1-C_4 alkoxy)carbonyl)-N-(C_1-C_4 alkyl)amino, hydroxy, C_1-C_4 alkoxy, aryl-C_1-C_2-alkoxy, heterocyclyl, aryl or heteroaryl radicals, wherein the heterocyclyl, aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_5 alkanoyl, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

(2) cycloalkyl or heterocyclyl radical optionally substituted by 1-2 radicals of (C_1-C_4 alkoxy)carbonyl, hydroxy or C_1-C_4 alkyl; or

(3) aryl or heteroaryl radicals optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

each R^{31} is independently hydrogen radical or R^{30}; and

wherein cycloalkyl is a monocyclic carbocyclic alkyl radical of 3-6 ring members, which is optionally partially unsaturated or benzo-fused; cycloalkylene is a monocyclic cycloalkyl gem divalent radical of 3-6 ring members; heterocyclyl is a radical of a monocyclic saturated heterocyclic ring system having 5-8 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally partially unsaturated or benzo-fused and optionally substituted by 1-2 oxo or thioxo radicals; heterocyclylene is a monocyclic heterocyclyl gem divalent radical on a ring carbon atom and having 5-6 ring members; aryl is a phenyl, biphenyl or naphthyl radical; and heteroaryl is radical of a monocyclic or bicyclic aromatic heterocyclic ring system having 5-6 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally benzo-fused or saturated C_3-C_4-carbocyclic-fused.

37. The compound of Claim 36 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_1-C_{12} alkyl or cycloalkyl radical optionally substituted by 1-2 radicals of -OH, $-OR^3$,

$-NR^3R^4$, aryl, heteroaryl or cycloalkyl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl and cycloalkyl radicals are optionally substituted by 1-2 radicals of hydroxy, $-OR^3$, $-SR^3$, $-S(O)_2R^3$, $-NR^3R^4$, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, halo, C_1-C_6 alkyl or $-CF_3$ radicals; provided that the total number of aryl, heteroaryl and cycloalkyl radicals in R^1 is 0-2;

wherein each R^3 is independently an C_1-C_4 alkyl, $-CF_3$, aryl, heteroaryl, aryl-C_1-C_2-alkyl or heteroaryl-C_1-C_2-alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, methylsulfonylamino, C_1-C_2 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, halo, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$;

V is $-CHR^{11}-$; wherein R^{11} is (1) a hydrogen, $-OR^{20}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, aryloxy, heteroaryloxy, C_1-C_2 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals;

wherein each R^{20} is independently a hydrogen, C_1-C_4 alkyl-C(O)R^{22}, C_2-C_4 alkenyl, cycloalkyl, aryl, heteroaryl, aryl-C_1-C_2-alkyl, heteroaryl-C_1-C_2-alkyl or C_1-C_4 alkanoyl; and wherein the cycloalkyl, aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

each R^{21} is independently an C_1-C_4 alkyl, C_1-C_4 alkyl-C(O)R^{22}, aryl, heteroaryl, aryl-C_1-C_2-alkyl or heteroaryl-C_1-C_2-alkyl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals;

wherein each R^{22} is independently a hydroxy or $-NR^{23}R^{24}$ radical; wherein R^{23} is a hydrogen, C_1-C_2 alkyl, aryl, aryl-C_1-C_2-alkyl, heteroaryl or heteroaryl-C_1-C_2-alkyl radical; and R^{24} is a hydrogen or C_1-C_2 alkyl radical; or $-NR^{23}R^{24}$ represents a heteroaryl radical; wherein the aryl and heteroaryl radicals of R^{22}, R^{23} and $-NR^{23}R^{24}$ are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

W-N represents $-C(O)-CR^{15}R^{16}-N$, $-CR^{15}R^{16}-N$ or $-CR^{17}R^{18}-CR^{15}R^{16}-N$; wherein R^{15} is (1) a hydrogen, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl radical optionally substituted with an $-OR^{20}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, C_1-C_4

alkoxycarbonylamino, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-2; and

R^{16} and R^{18} are each a hydrogen radical;

R^{17} is (1) a hydrogen, $-OR^{20}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl radical optionally substituted with an $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

wherein each B is independently a
(1) bond;
(2) C_1-C_4 alkyl radical; or
(3) aryl or heteroaryl radical optionally substituted by a radical of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_2 alkylsulfonylamino, hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthio, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

each A is independently a
(1) hydrogen radical;
(2) halo radical;
(3) $-C(O)-R^{30}$, $-C(O)-OR^{31}$, $-C(O)-NR^{32}R^{31}$ or $-C(NR^{32})-NR^{32}R^{31}$ radical;
(4) $-OR^{31}$ radical;

(5) $-SR^{31}$, $-S(O)_2-R^{30}$ or $-S(O)_2-NR^{32}R^{31}$ radical; or

(6) $-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$ or $-NR^{33}-S(O)_2-R^{30}$ radical;

wherein each R^{30} is independently

(1) heterocyclyl radical optionally substituted by 1-2 radicals of (C_1-C_4 alkoxy)carbonyl, hydroxy or C_1-C_4 alkyl; or

(2) heteroaryl radicals optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

each R^{31} is independently

(1) hydrogen or $-CF_3$ radical;

(2) C_1-C_4 alkyl radical optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy or aryl-C_1-C_2-alkoxy, aryl or heteroaryl radicals, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_5 alkanoyl, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

(3) cycloalkyl radical optionally substituted by 1-2 radicals of hydroxy or C_1-C_4 alkyl; or

(4) aryl or heteroaryl radicals optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals.

38. The compound of Claim 37 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_1-C_{12} alkyl or cycloalkyl radical optionally substituted by 1-2 radicals of -OH, -OR^3, -NR^3R^4, aryl or heteroaryl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl and cycloalkyl radicals are optionally substituted by 1-2 radicals of hydroxy, -OR^3, -SR^3, -$S(O)_2R^3$, -NR^3R^4, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, halo, C_1-C_6 alkyl or -CF_3 radicals; provided that the total number of aryl, heteroaryl and cycloalkyl radicals in R^1 is 0-1;

wherein each R^3 is independently an C_1-C_4 alkyl, -CF_3, aryl, heteroaryl, arylmethyl or heteroarylmethyl radical;

V is -CHR^{11}-; wherein R^{11} is (1) a hydrogen, -OR^{20}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-$S(O)_2$-R^{30}, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an -OR^{20}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-$S(O)_2$-R^{30}, aryl or heteroaryl radical;

wherein each R^{20} is independently a hydrogen, C_2-C_4 alkenyl, cycloalkyl, aryl, heteroaryl, aryl-C_1-C_2-alkyl, heteroaryl-C_1-C_2-alkyl or C_1-C_4 alkanoyl radical; and

W-N represents -C(O)-$CR^{15}R^{16}$-N, -$CR^{15}R^{16}$-N or -$CR^{17}R^{18}$-$CR^{15}R^{16}$-N; wherein R^{15} is (1) a hydrogen, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl radical optionally substituted with an aryl or heteroaryl radical; provided that the combined total number of

aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-2; and

R^{17} is a hydrogen, hydroxy or C_1-C_4 alkyl radical; and

X is S, Y is CR^9 and Z is N; or
Z is S, X is N and Y is CR^9;

wherein each B is independently a
(1) bond;
(2) C_1-C_4 alkyl radical; or
(3) aryl or heteroaryl radical;

each A is independently a
(1) hydrogen radical;
(2) halo radical; or
(3) $-C(O)-R^{30}$, $-C(O)-OR^{31}$ or $-C(O)-NR^{32}R^{31}$ radical;

wherein each R^{30} is independently a heterocyclyl radical optionally substituted by C_1-C_4 alkyl; and

each R^{31} is independently hydrogen radical or
(1) C_1-C_4 alkyl radical optionally substituted by 1-2 radicals of aryl or heteroaryl radicals, wherein the aryl and heteroaryl radicals are optionally substituted by a hydroxy, C_1-C_4 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radical; or
(2) cycloalkyl radical optionally substituted by 1-2 radicals of hydroxy or C_1-C_4 alkyl; or
(3) aryl or heteroaryl radicals optionally substituted by a hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radical.

39. The compound of Claim 38 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_5-C_{12} alkyl radical optionally substituted by 1-2 radicals of -OH, -OR^3 or -NR^3R^4; or (2) aryl or heteroaryl radicals optionally substituted by a hydroxy, -OR^3, -SR^3, -$S(O)_2R^3$, -NR^3R^4, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, halo, C_1-C_6 alkyl or -CF_3 radical; provided that the total number of aryl and heteroaryl radicals in R^1 is 0-1; and

wherein heterocyclyl is a radical of pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiamorpholinyl, 4-benzyl-piperazin-1-yl, pyrimidinyl, tetrahydrofuryl, pyrazolidonyl, pyrazolinyl, pyridazinonyl, pyrrolidonyl, tetrahydrothienyl or its sulfoxide or sulfone derivative, 2,3-dihydroindolyl, tetrahydroquinolinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydro-1-oxo-isoquinolinyl, 2,3-dihydrobenzofuryl, benzopyranyl, methylenedioxyphenyl or ethylenedioxyphenyl; aryl is a phenyl, biphenyl or naphthyl radical; and heteroaryl is radical of imidazolyl, pyrrolyl, pyrazolyl, pyridyl, pyrazinyl, triazolyl, furyl, thienyl, oxazolyl, thiazolyl, indolyl, quinolinyl, isoquinolinyl, 5,6,7,8-tetrahydroquinolyl, 5,6,7,8-tetrahydroisoquinolinyl, quinoxalinyl, benzothiazolyl, ß-carbolinyl, benzofuryl, benzimidazolyl or benzoxazolyl.

40. The compound of Claim 34 or a pharmaceutically acceptable salt thereof, wherein

V is -CHR^{11}-CHR^{12}-; wherein R^{11} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{12} is (1) a

hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; or wherein R^{12} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{11} is (1) a hydrogen, $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, $-NR^{33}-S(O)_2-NR^{32}R^{31}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, azido, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

W-N represents -C(O)-N or $-CR^{15}R^{16}$-N; wherein R^{15} is (1) a hydrogen, $-C(O)R^{22}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl, C_2-C_8 alkenyl or C_2-C_8 alkynyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, methylsulfinyl, methylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-3; and

R^{16} is a hydrogen radical; or $-CR^{15}R^{16}$- represents a cycloalkylene or heterocyclylene radical.

41. The compound of Claim 40 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_1-C_{12} alkyl or cycloalkyl radical optionally substituted by 1-3 radicals of -OH, $-OR^3$, $-SR^3$, $-S(O)_2R^3$, $-NR^3R^4$, aryl, heteroaryl, cycloalkyl or heterocyclyl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl, cycloalkyl and heterocyclyl radicals are optionally substituted by 1-3 radicals of hydroxy, $-OR^3$, $-SR^3$, $-S(O)_2R^3$, $-NR^3R^4$, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_6 alkyl or $-CF_3$ radicals; provided that the total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in R^1 is 0-2;

wherein each R^3 is independently an C_1-C_4 alkyl, -CF_3, aryl, heteroaryl, aryl-C_1-C_2-alkyl or heteroaryl-C_1-C_2-alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, cyano, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3;

V is -CHR^{11}-CHR^{12}-; wherein R^{11} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{12} is (1) a hydrogen, -OR^{20}, -SR^{21}, -C(O)R^{22}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-S(O)$_2$-R^{30}, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an -OR^{20}, -SR^{21}, -C(O)R^{22}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-S(O)$_2$-R^{30}, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, methylsulfonyl, halo, azido, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals; or wherein R^{12} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{11} is (1) a hydrogen, -OR^{20}, -SR^{21}, -C(O)R^{22}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-S(O)$_2$-R^{30}, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an -OR^{20}, -SR^{21}, -C(O)R^{22}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-S(O)$_2$-R^{30}, aryl or heteroaryl radical; wherein the aryl and

heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, aryloxy, heteroaryloxy, C_1-C_4 alkylthiol, methylsulfonyl, halo, azido, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals;

wherein each R^{22} is independently a hydroxy, C_1-C_4 alkoxy, aryloxy, aryl-C_1-C_2-alkoxy, heteroaryloxy, heteroaryl-C_1-C_2-alkoxy or -$NR^{23}R^{24}$ radical; wherein R^{23} is a hydrogen, C_1-C_4 alkyl, aryl, aryl-C_1-C_2-alkyl, heteroaryl or heteroaryl-C_1-C_2-alkyl radical; and R^{24} is a hydrogen or C_1-C_4 alkyl radical; or -$NR^{23}R^{24}$ represents a heterocyclyl or heteroaryl radical; wherein the heterocyclyl, aryl and heteroaryl radicals of R^{22}, R^{23} and -$NR^{23}R^{24}$ are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, halo, azido, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals; and

W-N represents -$CR^{15}R^{16}$-N; wherein R^{15} is (1) a hydrogen, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl radical optionally substituted with an -OR^{20}, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, C_1-C_4 alkoxycarbonylamino, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals; or -$CR^{15}R^{16}$- represents a cycloalkylene or heterocyclylene radical; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-2; and

R^{16} is a hydrogen radical;

wherein each B is independently a
(1) bond;
(2) C_1-C_4 alkyl radical optionally substituted by (a) a radical of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, hydroxy or C_1-C_2 alkoxy, and/or (b) 1-2 halo radicals, and/or (c) a radical of heterocyclyl, aryl or heteroaryl optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_2 alkylsulfonylamino, hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthio, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;
(3) heterocyclyl radical; or
(4) aryl or heteroaryl radical optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_2 alkylsulfonylamino, hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthio, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

each A is independently a
(1) hydrogen radical;
(2) halo radical;
(3) $-C(O)-R^{30}$, $-C(O)-OR^{31}$, $-C(O)-NR^{32}R^{31}$ or $-C(NR^{32})-NR^{32}R^{31}$ radical;
(4) $-OR^{31}$ radical;
(5) $-SR^{31}$, $-S(O)_2-R^{30}$ or $-S(O)_2-NR^{32}R^{31}$ radical; or
(6) $-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$ or $-NR^{33}-S(O)_2-NR^{32}R^{31}$ radical;

wherein each R^{30} is independently

(1) $-CF_3$ or C_1-C_4 alkyl radical optionally substituted by 1-2 radicals of $-CO_2R^{34}$, amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, N-((C_1-C_4 alkoxy)carbonyl)-N-(C_1-C_4 alkyl)amino, hydroxy, C_1-C_4 alkoxy or aryl-C_1-C_2-alkoxy, heterocyclyl, aryl or heteroaryl radicals, wherein the heterocyclyl, aryl and heteroaryl radicals are optionally substituted by 1-3 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_5 alkanoyl, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

(2) cycloalkyl or heterocyclyl radical optionally substituted by 1-2 radicals of (C_1-C_4 alkoxy)carbonyl, hydroxy or C_1-C_4 alkyl; or

(3) aryl or heteroaryl radicals optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

each R^{31} is independently hydrogen radical or R^{30}; and

wherein cycloalkyl is a monocyclic carbocyclic alkyl radical of 3-6 ring members, which is optionally partially unsaturated or benzo-fused; cycloalkylene is a monocyclic cycloalkyl gem divalent radical of 3-6 ring members; heterocyclyl is a radical of a monocyclic saturated heterocyclic ring system having 5-8 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally partially unsaturated or benzo-fused and optionally substituted by 1-2 oxo or thioxo radicals; heterocyclylene is a monocyclic heterocyclyl gem divalent radical on a ring carbon atom and having 5-6 ring members; aryl is a phenyl, biphenyl or naphthyl

radical; and heteroaryl is radical of a monocyclic or bicyclic aromatic heterocyclic ring system having 5-6 ring members per ring, wherein 1-3 ring members are oxygen, sulfur or nitrogen heteroatoms, which is optionally benzo-fused or saturated C_3-C_4-carbocyclic-fused.

42. The compound of Claim 41 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_1-C_{12} alkyl or cycloalkyl radical optionally substituted by 1-2 radicals of -OH, $-OR^3$, $-NR^3R^4$, aryl, heteroaryl and cycloalkyl; or (2) aryl or heteroaryl radicals; wherein the aryl, heteroaryl and cycloalkyl radicals are optionally substituted by 1-2 radicals of hydroxy, $-OR^3$, $-SR^3$, $-S(O)_2R^3$, $-NR^3R^4$, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, halo, C_1-C_6 alkyl or $-CF_3$ radicals; provided that the total number of aryl, heteroaryl and cycloalkyl radicals in R^1 is 0-2;

wherein each R^3 is independently an C_1-C_4 alkyl, $-CF_3$, aryl, heteroaryl, aryl-C_1-C_2-alkyl or heteroaryl-C_1-C_2-alkyl radical, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, methylsulfonylamino, C_1-C_2 alkylsulfonyl, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, halo, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$;

V is $-CHR^{11}-CHR^{12}-$; wherein R^{11} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{12} is (1) a

hydrogen, $-OR^{20}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, aryloxy, heteroaryloxy, C_1-C_2 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals; or wherein R^{12} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{11} is (1) a hydrogen, $-OR^{20}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an $-OR^{20}$, $-SR^{21}$, $-C(O)R^{22}$, $-O-C(O)-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$, $-NR^{33}-C(O)-OR^{30}$, $-NR^{33}-C(O)-NR^{32}R^{31}$, $-NR^{33}-S(O)_2-R^{30}$, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, aryloxy, heteroaryloxy, C_1-C_2 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals;

wherein each R^{20} is independently a hydrogen, C_1-C_4 alkyl-$C(O)R^{22}$, C_2-C_4 alkenyl, cycloalkyl, aryl, heteroaryl, aryl-C_1-C_2-alkyl, heteroaryl-C_1-C_2-alkyl or C_1-C_4 alkanoyl; and wherein the cycloalkyl, aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, halo, azido, C_1-C_2 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

each R^{21} is independently an C_1-C_4 alkyl, C_1-C_4 alkyl-C(O)R^{22}, aryl, heteroaryl, aryl-C_1-C_2-alkyl or heteroaryl-C_1-C_2-alkyl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthiol, halo, azido, C_1-C_2 alkyl, -CF_3 or -OCF_3 radicals;

wherein each R^{22} is independently a hydroxy or -$NR^{23}R^{24}$ radical; wherein R^{23} is a hydrogen, C_1-C_2 alkyl, aryl, aryl-C_1-C_2-alkyl, heteroaryl or heteroaryl-C_1-C_2-alkyl radical; and R^{24} is a hydrogen or C_1-C_2 alkyl radical; or -$NR^{23}R^{24}$ represents a heteroaryl radical; wherein the aryl and heteroaryl radicals of R^{22}, R^{23} and -$NR^{23}R^{24}$ are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, halo, azido, C_1-C_2 alkyl, -CF_3 or -OCF_3 radicals; and

W-N represents -$CR^{15}R^{16}$-N; wherein R^{15} is (1) a hydrogen, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl, radical optionally substituted with an -OR^{20}, aryl or heteroaryl radical; wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthiol, amino, acetylamino, C_1-C_4 alkoxycarbonylamino, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-2; and

R^{16} is a hydrogen radical;

wherein each B is independently a
(1) bond;

(2) C_1-C_4 alkyl radical; or

(3) aryl or heteroaryl radical optionally substituted by a radical of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4 alkoxy)carbonylamino, C_1-C_2 alkylsulfonylamino, hydroxy, C_1-C_2 alkoxy, C_1-C_2 alkylthio, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals;

each A is independently a

(1) hydrogen radical;

(2) halo radical;

(3) $-C(O)-R^{30}$, $-C(O)-OR^{31}$, $-C(O)-NR^{32}R^{31}$ or $-C(NR^{32})-NR^{32}R^{31}$ radical;

(4) $-OR^{31}$ radical;

(5) $-SR^{31}$, $-S(O)_2-R^{30}$ or $-S(O)_2-NR^{32}R^{31}$ radical; or

(6) $-NR^{32}R^{31}$, $-NR^{33}-C(O)-R^{31}$ or $-NR^{33}-S(O)_2-R^{30}$ radical;

wherein each R^{30} is independently

(1) heterocyclyl radical optionally substituted by 1-2 radicals of (C_1-C_4 alkoxy)carbonyl, hydroxy or C_1-C_4 alkyl; or

(2) heteroaryl radicals optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

each R^{31} is independently

(1) hydrogen or $-CF_3$ radical;

(2) C_1-C_4 alkyl radical optionally substituted by 1-2 radicals of hydroxy, C_1-C_2 alkoxy or aryl-C_1-C_2-alkoxy, aryl or heteroaryl radicals, wherein the aryl and heteroaryl radicals are optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, (C_1-C_4

alkoxy)carbonylamino, C_1-C_5 alkanoyl, (C_1-C_4 alkoxy)carbonyl, hydroxy, C_1-C_4 alkoxy, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals;
(3) cycloalkyl radical optionally substituted by 1-2 radicals of hydroxy or C_1-C_4 alkyl; or
(4) aryl or heteroaryl radicals optionally substituted by 1-2 radicals of amino, C_1-C_2 alkylamino, di-(C_1-C_2 alkyl)amino, C_1-C_2 alkanoylamino, hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, -CF_3 or -OCF_3 radicals.

43. The compound of Claim 42 or a pharmaceutically acceptable salt thereof, wherein

R^1 is (1) an C_5-C_{12} alkyl radical optionally substituted by 1-2 radicals of -OH, -OR^3 or -NR^3R^4; or (2) aryl or heteroaryl radicals optionally substituted by a hydroxy, -OR^3, -SR^3, -$S(O)_2R^3$, -NR^3R^4, amino, acetylamino, methylsulfonylamino, C_1-C_4 alkoxycarbonylamino, C_1-C_4 alkoxycarbonyl, halo, C_1-C_6 alkyl or -CF_3 radicals; provided that the total number of aryl, heteroaryl and cycloalkyl radicals in R^1 is 0-1;

wherein each R^3 is independently an C_1-C_4 alkyl, -CF_3, aryl, heteroaryl, arylmethyl or heteroarylmethyl radical;

V is -CHR^{11}-CHR^{12}-; wherein R^{11} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{12} is (1) a hydrogen, -OR^{20}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-$S(O)_2$-R^{30}, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an -OR^{20}, -

O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-$S(O)_2$-R^{30}, aryl or heteroaryl radical; or wherein R^{12} is a hydrogen, hydroxy, C_1-C_4 alkoxy or C_1-C_4 alkyl radical and R^{11} is (1) a hydrogen, -OR^{20}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-$S(O)_2$-R^{30}, aryl or heteroaryl radical; or (2) an C_1-C_8 alkyl or C_2-C_8 alkenyl radical optionally substituted with an -OR^{20}, -O-C(O)-$NR^{32}R^{31}$, -NR^{33}-C(O)-R^{31}, -NR^{33}-C(O)-OR^{30}, -NR^{33}-C(O)-$NR^{32}R^{31}$, -NR^{33}-$S(O)_2$-R^{30}, aryl or heteroaryl radical;

wherein each R^{20} is independently a hydrogen, C_2-C_4 alkenyl, cycloalkyl, aryl, heteroaryl, aryl-C_1-C_2-alkyl, heteroaryl-C_1-C_2-alkyl or C_1-C_4 alkanoyl radical; and

W-N represents -$CR^{15}R^{16}$-N; wherein R^{15} is (1) a hydrogen, aryl or heteroaryl radical; or (2) an C_1-C_4 alkyl, radical optionally substituted with an aryl or heteroaryl radical; provided that the combined total number of aryl, heteroaryl, cycloalkyl and heterocyclyl radicals in V and W is 0-2; and

X is S, Y is CR^9 and Z is N; or
Z is S, X is N and Y is CR^9;

wherein each B is independently a
(1) bond;
(2) C_1-C_4 alkyl radical; or
(3) aryl or heteroaryl radical;

each A is independently a
(1) hydrogen radical;

(2) halo radical; or
(3) $-C(O)-R^{30}$, $-C(O)-OR^{31}$ or $-C(O)-NR^{32}R^{31}$ radical;

wherein each R^{30} is independently
(1) heterocyclyl radical optionally substituted by C_1-C_4 alkyl;

each R^{31} is independently hydrogen radical or
(1) C_1-C_4 alkyl radical optionally substituted by 1-2 radicals of aryl or heteroaryl radicals, wherein the aryl and heteroaryl radicals are optionally substituted by a hydroxy, C_1-C_4 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; or
(2) cycloalkyl radical optionally substituted by 1-2 radicals of hydroxy or C_1-C_4 alkyl; or
(3) aryl or heteroaryl radicals optionally substituted by a hydroxy, C_1-C_2 alkoxy, halo, C_1-C_4 alkyl, $-CF_3$ or $-OCF_3$ radicals; and

wherein heterocyclyl is a radical of pyrrolidinyl, piperidinyl, piperazinyl, morpholinyl, thiamorpholinyl, 4-benzyl-piperazin-1-yl, pyrimidinyl, tetrahydrofuryl, pyrazolidonyl, pyrazolinyl, pyridazinonyl, pyrrolidonyl, tetrahydrothienyl or its sulfoxide or sulfone derivative, 2,3-dihydroindolyl, tetrahydroquinolinyl, 1,2,3,4-tetrahydroisoquinolinyl, 1,2,3,4-tetrahydro-1-oxo-isoquinolinyl, 2,3-dihydrobenzofuryl, benzopyranyl, methylenedioxyphenyl or ethylenedioxyphenyl; aryl is a phenyl, biphenyl or naphthyl radical; and heteroaryl is radical of imidazolyl, pyrrolyl, pyrazolyl, pyridyl, pyrazinyl, triazolyl, furyl, thienyl, oxazolyl, thiazolyl, indolyl, quinolinyl, isoquinolinyl, 5,6,7,8-tetrahydroquinolyl, 5,6,7,8-tetrahydroisoquinolinyl, quinoxalinyl, benzothiazolyl, ß-carbolinyl, benzofuryl, benzimidazolyl or benzoxazolyl.

44. The compound of Claim 1 which is:

5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6(R)-hyrdoxamic acid;

5-(4-methoxybenzenesulfonyl)-4,5,6,7-tetrahydro-7-acetoxy-thieno[3,2-c]pyridine-6-hydroxamic acid;

5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-7-hydroxy-thieno[3,2-c]pyridine-6-hydroxamic acid;

7-(N-benzylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid;

7-(N-phenylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid;

7-(N-methylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid;

7-(N-isopropylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid;

7-(N-(4-phenoxyphenyl)aminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid;

7-(N-(1-phenylethyl)aminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid;

7-(N-(4-methoxyphenyl)aminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid;

7-(N-(phenethyl)aminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid;

7-(N-cyclohexylaminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid;

7-(N-(2-biphenyl)aminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid;

7-(N-(4-butoxycarbonylphenyl) aminocarbonyloxy)-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid;

7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-benzyl-N-methylaminocarbonyl)-4,5,6,7-tetrahydro thieno-[3,2-c]-pyridinyl-6-hydroxamic acid;

7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-phenyl-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid;

7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(methoxycarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid;

7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-carboxy-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid;

7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(ethoxycarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid;

7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(2-pyridyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid;

7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(3-pyridyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridinyl-6-hydroxamic acid;

7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(4-morpholinocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid;

7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(phenylmethoxycarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid;

7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-phenylaminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid;

7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-benzylaminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid;

7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-(3-phenylpropyl)aminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid;

7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-methyl-N-(phenethyl)aminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid;

7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-benzyl-N-ethylaminocarbonyl)-4,5,6,7-tetrahydro thieno-[3,2-c]-pyridine-6-hydroxamic acid;

7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-(4,4-dimethylpentyl)aminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid;

7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-(4,4-diphenylbutyl)aminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid;

7-hydroxy-5-(4-methoxyphenylsulfonyl)-2-(N-phenyl-N-methylaminocarbonyl)-4,5,6,7-tetrahydrothieno-[3,2-c]-pyridine-6-hydroxamic acid;

4-benzyl-6-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[2,3,-c]pyridine-5-hydroxamic acid;

4-benzyl-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid;

7-benzyl-8-cis-hydroxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[3,4,d]azepine-5-hydroxamic acid;

4-hydroxy-6-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-5-hydroxamic acid;

2-carboxy-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-6-hydroxamic acid;

5-(4-methoxyphenylsulfonyl)-2-pyrid-2-yl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-hydroxamic acid;

5-(4-methoxyphenylsulfonyl)-2-pyrid-2-yl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-hydroxamic acid;

4-hydroxy-3-benzyl-4-hydroxy-6-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-5-hydroxamic acid;

4-hydroxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid;

4-hydroxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid;

4-(2-(3,5-dimethylphenyl) ethyl)-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid;

6-(4-methoxyphenylsulfonyl)-4-phenethyl-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid;

6-(4-methoxyphenylsulfonyl)-4-[2-(4-trifluoromethyl phenyl)ethyl]-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid;

4-[2-(4-chlorophenyl)ethyl]-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid;

6-(4-methoxyphenylsulfonyl)-4-[2-(4-methoxyphenyl)ethyl]-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid;

6-(4-methoxyphenylsulfonyl)-4-[2-(3-methoxyphenyl)ethyl]-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid;

6-(4-methoxyphenylsulfonyl)-4-(4-phenylbut-3-enyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid;

6-(4-methoxyphenylsulfonyl)-4-(3-methylbut-3-enyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid;

6-(4-methoxyphenylsulfonyl)-4-(3-methylbutyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid;

4-[2-(3-hydroxymethylphenyl)ethyl]-6-(4-methoxyphenyl sulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid;

6-(4-methoxyphenylsulfonyl)-4-(2-methoxyethyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid;

4-[2-hydroxyethyl]-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid;

6-(4-methoxyphenylsulfonyl)-4-vinyl-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid;

6-(4-methoxyphenylsulfonyl)-4-(phenylsulfanylmethyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid;

4-hydroxymethyl-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-5-hydroxamic acid;

4-hydroxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-hydroxamic acid;

4-methoxy-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-hydroxamic acid;

6-(4-methoxyphenylsulfonyl)-4-oxo-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-hydroxamic acid;

6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-hydroxamic acid;

3-benzyl-6-(4-methoxyphenylsulfonyl)-5,6,7,8-tetrahydro-4H-thieno[2,3-d]azepine-7-hydroxamic acid;

3-benzyl-6-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[2,3-c]pyridine-5-hydroxamic acid;

5-(4-methoxyphenyl sulfonyl)-4-phenethyl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-hyrdoxamic acid;

5-(4-methoxyphenylsulfonyl)-4-methyl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-hydroxamic acid;

5-(4-methoxyphenylsulfonyl)-4-methyl-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-hydroxamic acid; or

4-benzyl-5-(4-methoxyphenylsulfonyl)-4,5,6,7-tetrahydro-thieno[3,2-c]pyridine-6-hydroxamic acid.

45. A pharmaceutical composition comprising a compound of Claims 1-44 and a pharmaceutically acceptable carrier.

46. A method for prophylaxis or treatment of inflammation comprising administering an effective amount of a compound of Claims 1-44.

47. A method for prophylaxis or treatment of inflammation comprising administering an effective amount of a composition of Claim 45.

48. A method for prophylaxis or treatment of connective tissue degradation comprising administering an effective amount of a compound of Claims 1-44.

49. A method for prophylaxis or treatment of connective tissue degradation comprising administering an effective amount of a composition of Claim 45.

50. A method of treating rheumatoid arthritis; osteoarthritis; rheumatoid spondylitis; gouty arthritis;

inflammatory bowel disease; adult respiratory distress syndrome (ARDS); psoriasis; Crohn's disease; allergic rhinitis; ulcerative colitis; anaphylaxis; contact dermatitis; asthma; HIV infections; cytomegalovirus (CMV) infections; influenza; adenovirus infections; herpesvirus infections; herpes zoster; muscle degeneration; cachexia; Reiter's syndrome; type II diabetes; bone resorption diseases; graft vs. host reaction; ischemia reperfusion injury; atherosclerosis; brain trauma; Alzheimer's disease; multiple sclerosis; cerebral malaria; sepsis; septic shock; toxic shock syndrome; or fever or mylagias due to infection comprising administering an effective amount of a compound of Claims 1-44.

51. A method of treating rheumatoid arthritis; osteoarthritis; rheumatoid spondylitis; gouty arthritis; inflammatory bowel disease; adult respiratory distress syndrome (ARDS); psoriasis; Crohn's disease; allergic rhinitis; ulcerative colitis; anaphylaxis; contact dermatitis; asthma; HIV infections; cytomegalovirus (CMV) infections; influenza; adenovirus infections; herpesvirus infections; herpes zoster; muscle degeneration; cachexia; Reiter's syndrome; type II diabetes; bone resorption diseases; graft vs. host reaction; ischemia reperfusion injury; atherosclerosis; brain trauma; Alzheimer's disease; multiple sclerosis; cerebral malaria; sepsis; septic shock; toxic shock syndrome; or fever or mylagias due to infection comprising administering an effective amount of a composition of Claim 45.

52. A method of lowering plasma concentrations of TNF-α comprising administering an effective amount of a compound of Claims 1-44.

53. A method of lowering plasma concentrations of TNF-α comprising administering an effective amount of a composition of Claims 1-44.

54. Use of a compound of Claims 1-44 for a medicament.

55. Use of a compound of Claims 1-44 for prophylaxis or treatment of inflammation.

56. Use of a composition of Claim 45 for prophylaxis or treatment of inflammation.

57. Use of a compound of Claims 1-44 for prophylaxis or treatment of connective tissue degradation.

58. Use of a composition of Claim 45 for prophylaxis or treatment of connective tissue degradation.

59. Use of a compound of Claims 1-44 for prophylaxis or treatment of rheumatoid arthritis; osteoarthritis; rheumatoid spondylitis; gouty arthritis; inflammatory bowel disease; adult respiratory distress syndrome (ARDS); psoriasis; Crohn's disease; allergic rhinitis; ulcerative colitis; anaphylaxis; contact dermatitis; asthma; HIV infections; cytomegalovirus (CMV) infections; influenza; adenovirus infections; herpesvirus infections; herpes zoster; muscle degeneration; cachexia; Reiter's syndrome; type II diabetes; bone resorption diseases; graft vs. host reaction; ischemia reperfusion injury; atherosclerosis; brain trauma; Alzheimer's disease; multiple sclerosis; cerebral malaria; sepsis; septic shock; toxic shock syndrome; or fever or mylagias due to infection.

60. Use of a composition of Claim 45 for the prophylaxis or treatment of rheumatoid arthritis; osteoarthritis; rheumatoid spondylitis; gouty arthritis; inflammatory bowel disease; adult respiratory distress syndrome (ARDS); psoriasis; Crohn's disease; allergic rhinitis; ulcerative colitis; anaphylaxis; contact dermatitis; asthma; HIV infections; cytomegalovirus (CMV) infections; influenza; adenovirus infections; herpesvirus infections; herpes zoster; muscle degeneration; cachexia; Reiter's syndrome; type II diabetes; bone resorption diseases; graft vs. host reaction; ischemia reperfusion injury; atherosclerosis; brain trauma; Alzheimer's disease; multiple sclerosis; cerebral malaria; sepsis; septic shock; toxic shock syndrome; or fever or mylagias due to infection.

61. Use of a compound of Claims 1-44 for preparing a medicament.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 98/16147

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07D495/04 A61K31/44 A61K31/55 C07D491/048 C07D498/04
C07D513/04 //(C07D495/04,333:00,221:00),(C07D495/04,333:00,
223:00),(C07D495/04,333:00,225:00)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 18194 A (HOECHST) 22 May 1997 cited in the application see claims 1,8 ---	1,45,46
P,X	EP 0 803 505 A (ADIR) 29 October 1997 see claims 1,15;examples 1,15-19,28,30,38-45,50-53 see claim 1; examples 1,15-19,28,30 -----	1,45,48

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
5 November 1998	18/11/1998

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Alfaro Faus, I

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 98/16147

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 46 to 60
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 46 to 60 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Interr. ıal Application No
PCT/US 98/16147

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9718194 A	22-05-1997	DE 19542189 A	15-05-1997
		DE 19612298 A	02-10-1997
		AU 7562496 A	05-06-1997
		CZ 9801453 A	12-08-1998
		EP 0861236 A	02-09-1998
EP 803505 A	29-10-1997	FR 2748026 A	31-10-1997
		AU 1912197 A	30-10-1997
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		CN 1165817 A	26-11-1997
		JP 10059936 A	03-03-1998
		NO 971862 A	27-10-1997
		PL 319684 A	27-10-1997